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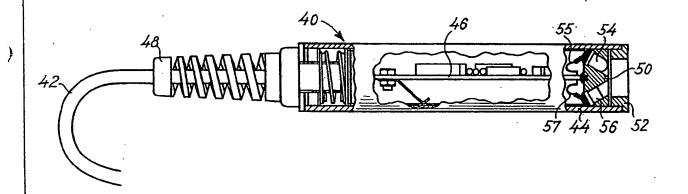
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(54) Title: A METHOD AND AN APPARATUS FOR DETERMINING AN INDIVIDUAL'S ABILITY TO STAND EXPOSURE TO ULTRAVIOLET RADIATION



(57) Abstract

A method and an apparatus for determining an individual's ability to become tanned or to stand exposure to ultraviolet radiation without causing a skin reaction, such as skin cancer or erythema. According to the method, at least part of said individual's skin surface is exposed to electromagnetic radiation of first and second wavelengths and of predetermined intensities. The first and second wavelengths at which erythrodermic skin reflection is high and low, respectively. The intensity of electromagnetic radiation reflected from the individual's skin surface is measured so as to determine first and second coefficients of reflection of said first and second wavelengths, respectively. The first and second coefficients are compared to sets of coefficients of reflection representing coherent sets of coefficients of reflection of specific states of redness, and the first and second coefficients of reflection are corrected into a set of corrected first and second coefficients of reflection of reflection is further converted into a measure representing the individual's ability to become tanned or to stand exposure to ultraviolet radiation without causing said skin reaction.

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A method and an apparatus for determining an individual's ability to stand exposure to ultraviolet radiation.

The present invention relates to the technique of determining an 5 individual's ability to become tanned or to stand exposure to ultraviolet radiation without causing a skin reaction, such as skin cancer or erythema, which technique is described in US Patent No. 4.882.598, to which US Patent reference is made, and which US Patent is herewith incorporated in the present specification by reference.

According to the technique described in the above US Patent, the individual's ability to become tanned or to stand exposure to ultraviolet radiation without causing a skin reaction may be determined by exposing a skin surface part of the individual to electromagnetic radiation, e.g. visible light, and determining the coefficient of reflection 15 of the individual's skin surface part to the electromagnetic radiation and converting the coefficient of reflection to a measure representing the individual's ability to become tanned or to stand exposure to ultraviolet radiation. The technique described in the above US Patent is based on clinical experiments revealing a linear relationship between a 20 number of individuals coefficients of skin surface reflection in logarithmic representation and the same individuals' ability to stand exposure to ultraviolet radiation of a predetermined intensity and of a predetermined spectral composition. According to the above-mentioned US Patent, individuals who are erythrodermic or erythematous may further be 25 identified by performing the determination of the individuals' coefficient of reflection to electromagnetic radiation at two distinct wavelengths, one of which is a wavelength at which erythrodermic skin reflection is high, and another one of which is a wavelength at which erythrodermic skin reflection is low.

The basis of the present invention is the realization that the determination of the individual's coefficient of reflection or reflections to electromagnetic radiation is to a high degree influenced by the blood flow of the individual at the site or the skin surface part at which the measurement is carried out. An obvious solution solving the problem of 35 eliminating the blood flow influence on the determination of the measure representing the individual's ability to become tanned or to stand exposure to ultraviolet radiation in accordance with the teaching of the above US Patent is to specify a "normal" measuring routine involving that the individual is kept in a normalized position and state, e.g.

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specifying the site or the part of the individual's skin surface at which the measurement is to be performed, the position of the site or skin surface part in question, and the position of the individual and further a specific increased or reduced blood flow accomplished through an occlusion of a body part of the individual, on which body part the site or skin surface part is positioned, or alternatively a state of extreme blood flow, e.g. provoked through heating the site or the skin surface part at which the measurement is to be performed. In numerous instances, the individuals cannot be maintained in a normalized position 10 and state corresponding to the above specified circumstances or similar relevant specified circumstances for numerous reasons. Also, a so-called normalized state may often result in an extreme variation of the measuring results obtained, which makes the overall measuring technique unreliable and inadequate.

An object of the present invention is to provide a method of de-15 termining an individual's ability to become tanned or to stand exposure to ultraviolet radiation without causing a skin reaction, which method is independent of the blood flow of the individual, and which method renders it possible to provide a measure representing said individual's ability independent on the blood flow of the individual.

A further object of the present invention is to provide a method of determining an individual's ability to become tanned or to stand exposure to ultraviolet radiation, which method produces normalized measuring results which are readily comparable, rendering it possible to ob-25 tain a high degree of reproducibility of the determination.

A further object of the present invention is to provide an apparatus for determining an individual's ability to become tanned or to stand exposure to ultraviolet radiation, which apparatus is capable to perform a measuring routine and generate a measuring result independent of the 30 blood flow of the individual, the ability of which is to be determined.

A still further object of the present invention is to provide an apparatus of the above type of an extreme reliability and producing measuring results of high reproducibility and high accuracy.

According to a first aspect of the present invention, a method of determining an individual's ability to become tanned or to stand exposure to ultraviolet radiation without causing a skin reaction, such as skin cancer or erythema, comprising the following steps:

exposing at least part of said individual's skin surface to

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electromagnetic radiation of a first wavelength and of a predetermined intensity, said first wavelength being a wavelength at which erythrodermic skin reflection is high,

measuring the intensity of electromagnetic radiation reflected from said part of said individual's skin surface so as to determine a first coefficient of reflection of said skin surface part to said electromagnetic radiation of said first wavelength,

exposing said skin surface part to electromagnetic radiation of a second wavelength and of a predetermined intensity, said second wavelength being a wavelength at which erythrodermic skin reflection is low,

measuring the intensity of electromagnetic radiation reflected from said part of said individual's skin surface part so as to determine a second coefficient of reflection of said skin surface part to electromagnetic radiation of said second wavelength,

comparing said first and second coefficients of reflection with sets of coefficients of reflection representing coherent sets of coefficients of reflection of said first and second wavelengths of specific states of redness so as to determine said individual's skin surface part's state of redness, converting said first and second coefficients 20 of reflection into a set of corrected first and second coefficients of reflection of a specific state of redness, so as to determine said individual's skin surface part's coefficients of reflection of said first and second wavelengths at a specific state of redness, and

converting said corrected first coefficient of reflection into a measure representing said individual's ability to become tanned or to stand exposure to ultraviolet radiation without causing said skin reaction.

Basically, in accordance with the teaching of the present invention, it has been realized through clinical investigations that the 30 first and the second coefficients of reflection determined in accordance with the teaching of the above US Patent may be converted to a set of corrected first and second coefficients of reflection of a specific state of redness since the first and the second coefficients of reflection at different states of redness, and consequently different blood 35 flows, fulfil specific mathematic relations, as will be evident from the description below, rendering it possible to convert a set of first and second coefficients of reflection to a set of corrected first and second coefficients of reflection of a specific state of redness. Preferably,

according to the teaching of the present invention, the specific state of redness to which the first and second coefficients of reflections measured in accordance with the method according to the present invention and in accordance with the teaching of the above US Patent corresponds to an average zero blood flow state, i.e. a state in which the individual's blood flow is zero or extremely low, eliminating to any substantial extent the influence of the redness of the individual on the coefficients of reflection.

According to a further realization according to the teaching of the present invention, the method advantageously further comprises the step of determining the individual's skin surface part's degree of pigmentation from the corrected first and second coefficients of reflection of the first and second wavelengths at the specific state of redness.

The basic clinical investigations on which the present invention is based have revealed that provided the coefficient of reflection of said second wavelength is represented in logarithmic representation, the mathematic relation through which sets of coefficients of reflection representing coherent sets of coefficients of reflection of said first and second wavelengths are linearly related, rendering the conversion of the first and the second coefficients of reflection into a set of coherent first and second coefficients of reflection extremely simple and readily adaptable to automatized conversion, e.g. by means of a computer, such as a microprocessor.

In accordance with a second aspect of the present invention, an apparatus is provided for determining an individual's ability to become tanned or to stand exposure to ultraviolet radiation without causing a skin reaction, such as skin cancer or erythema, comprising:

a first electromagnetic source for generating electromagnetic radiation of a first wavelength and of a predetermined intensity and for directing said electromagnetic radiation of said first wavelength to a part of said individual's skin surface so as to expose said part of said individual's skin surface to said electromagnetic radiation of said first wavelength,

a second electromagnetic source for generating electromagnetic ra-35 diation of a'second wavelength and of a predetermined intensity and for directing said electromagnetic radiation of said second wavelength to said part of said individual's skin surface so as to expose said part of said individual's skin surface to said electromagnetic radiation of said second wavelength,

a light-detecting means for measuring the intensity of electromagnetic radiation reflected from said part of said individual's skin surface,

a measuring means connected to said light-detecting means for measuring the intensity of electromagnetic radiation reflected from said part of said individual's skin surface so as to determine a first and a second coefficient of reflection of said skin surface part to said electromagnetic radiation of said first and second wavelength, respectively,

a comparison and converting means connected to said measuring means for comparing said first and second coefficients of reflection with sets of coefficients of reflection representing coherent sets of coefficients of reflection of said first and second wavelengths of specific states of redness so as to determine said individual's skin surface part's state of redness, for converting said first and second coefficients of reflection into a set of corrected first and second coefficients of reflection of a specific state of redness, so as to determine said individual's skin surface part's coefficients of reflection of said first and second wavelengths at a specific state of redness, and for converting said corrected first coefficient of reflection into a measure representing said individual's ability to become tanned or to stand exposure to ultraviolet radiation without causing said skin reaction.

Basically, the apparatus according to the present invention may be implemented in accordance with the above embodiments of the method according to the present invention. Furthermore, according to a first embodiment of the apparatus, separate light detector means for detecting electromagnetic radiation of the first and the second wavelengths, respectively, may be provided. Preferably, the apparatus according to the present invention, however, comprises a single light-detecting means constituted by a single light detector, first of all simplifying the structure of the apparatus and secondly ensuring that the reflection of light of the first and the second wavelength is generated at one and the same part of the individual's skin surface and further eliminates any difference in sensitivity and consequently measuring accuracy between the measurement of the reflection of electromagnetic radiation of the first and the second wavelength.

Due to the high accuracy of the measuring technique according to

the present invention, the UV treatment of e.g. psoriasis patients may be adapted so as to carry out a full-body scanning of the body of the patient for carrying out an optimum UV treatment of the entire body of the patient, at which treatment, any differences as to UV sensitivity of different skin surface areas of the patient are complied with, so that, independent of the difference in UV sensitivity of the difference skin surface areas of the patient, any skin surface area of the patient is exposed to an optimum UV treatment.

The present invention will now be further described with reference to the drawings, in which

Fig. 1 is a diagram illustrating the correspondence between the coefficient of skin surface reflection and the wavelength of the electromagnetic radiation, to which the skin surface part has been exposed, further illustrating a curve A illustrating the response of an average, non-sun-tanned and non-erythrodermic skin surface part of an individual and a curve B illustrating the response of an erythrodermic or sun-burnt skin surface part of an individual,

Fig. 2 is a diagram illustrating the correspondence between the coefficient of skin surface reflection and the wavelength of the electromagnetic radiation, to which the skin surface part has been exposed, further illustrating the same curve A as shown in Fig. 1 and a curve C illustrating the response of a non-erythrodermic and extremely pigmented skin surface part of an individual,

Fig. 3 is a diagram illustrating the linear relationship between the logarithmic representation of a number of individuals' coefficients of skin surface reflection and the individuals' ability to stand exposure to ultraviolet radiation of a predetermined intensity and of a predetermined specific spectral composition,

Fig. 4 is an overall schematic and perspective view of an apparatus 30 implemented in accordance with the teaching of the present invention,

Fig. 5A is an overall schematic and partly cut-away view of a photodetector constituting a component of the apparatus shown in Fig. 4,

Figs. 5B and 5C are elevational views of an optic guide and light diode and light detector supporting component of the photodetector shown in Fig. 5A.

Fig. 6 is a diagram illustrating the relation between measurements carried out on a total of 49 individuals, further illustrating the correspondence between the coefficient of reflection to red light and the

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coefficient of reflection to green light in logarithmic representation in dependency of the blood flow,

- Fig. 7 is a diagram similar to the diagram shown in Fig. 6, from which diagram an individual's corrected coefficient of reflection to red light and the same individual's pigmentation may be determined from a set of measuring results and related to a specific state of redness,
- Fig. 8 is a diagram similar to the diagrams of Figs. 6 and 7, illustrating the relation between the coefficient of reflection to red light and the coefficient of reflection to green light in logarithmic representation of individuals of different degrees of redness caused by ultraviolet radiation.
- Fig. 9a is a diagram illustrating the relation between the correspondence between the corrected coefficient of reflection to red light in logarithmic representation of individuals and the UV dose in B-MED of the same individuals.
  - Fig. 9b is a diagram illustrating the relation between the correspondence between the pigment% and the UV-dose in B-MED of the same individuals,
- Fig. 10 is a diagram illustrating the linear correspondence between 20 clinically evaluated redness of individuals and the degree of redness of the same individuals,
  - Fig. 11 is a circuit diagram of the electronic circuitry of the apparatus shown in Fig. 4,
- Fig. 12 A and B are circuit diagrams of a microprocessor block of the electronic circuitry shown in Fig. 11,
  - Fig. 13 is a circuit diagram of the electronic circuitry of the photodetector shown in Fig. 5,
- Fig. 14 is a diagram illustrating the linear relation between laser-induced skin changes of individuals subjected to laser treatment and the degree of pigmentation of the same individuals,
  - Fig. 15A-15L are diagrams further illustrating the correspondence between the laser-induced effects and the degree of pigmentation of the individuals exposed to laser treatment,
- Fig. 16 a diagram illustrating the linear relationship between in-35 dividuals' basic MEDs after UV treatment and the degree of pigmentation of the same individuals,
  - Fig. 17 is a diagram illustrating the difference between an experimentally found dose and a calculated dose to reach a certain degree of

redness, and

Fig. 18 is a diagram illustrating the difference of an individual's sensitivity to UV treatment compared to a normal sensitivity.

According to the present invention, non-invasive measuring techniques for measuring pigmentation and redness of a skin surface part of an individual are provided. Basically, the present invention constitutes a refinement or improvement of the technique described in US Patent No. 4.288.598, to which US Patent reference is made and which US Patent is herewith incorporated in the present specification by reference. Accord-10 ing to the non-invasive measuring technique according to the above US Patent and according to the present invention, a conversion from pigmentation to UV-sensitivity is established and an objective measurement of pigmentation and redness is provided, which objective measurement may be converted into UV-sensitivity of the individual in question. According 15 to the teachings of the present invention, phototherapy and photochemotherapy during treatment is adjustable so as to optimize the treatment of an individual at all times, taking into due consideration the action spectra for phototherapy and photochemotherapy.

The basic teachings of the present invention are based on the below 20 described measurements.

Spectrophotometric measurements of the reflection of skin surface parts of individuals were carried out within the wavelength area 260 nm - 800 nm. A laboratory system comprising a 150 W Xenon arc lamp (manufactured by Zeiss, FRG) was used irradiating the entrance slit of a 25 single grating monochromator (manufactured by Jobin-Yvon H20, France, 200 nm focal length, f/3.5). An 8 nm band-pass filter was used for all measurements. From the exit slit of the monochromator the light beam was directed to the skin surface part of an individual via one branch of a fused silica bifurcated fiber optic cable (manufactured by Oriel, Strat-30 ford, CT, USA). Said one branch of the fiber optic cable was held perpendicular to the skin surface part at a distance of 5 mm by means of a spacer device. The other branch of the fiber optic cable was used for directing the radiation reflected from the skin surface part to a calibrated multiprobe (manufactured by EG & G 550 - 2) connected to a 35 radiometer (manufactured by EG & G 550, Salem, MA, USA). The measurements were performed at every second nm from 260 nm to 800 nm using the reflection from a calcium carbonate plate as the 100% reflection reference at all wavelengths. On the basis of the measurements, spectra

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were recorded, and calculations based on the measurements were performed by a HP computer (manufactured by Hewlett Packard, Palo Alto, CA, USA).

A total of 22 individuals were used for recording reflection spectra, which 22 individuals had different skin complexion. Within the skin surface areas of the 22 individuals within which skin surface areas the measurements were performed, the MED (Minimum Erythema Dose for an individual person 24 h after exposure) was determined using the radiation from a Solar Simulator (manufactured by Solar Light Company, Philadelphia, PA, USA). Spots of a diameter of 1 cm were irradiated, and the redness of the skin surface parts was classified as one MED when minimal redness had clearly demarcation lines to the surrounding non-irradiated skin.

For all 22 individuals, spectra were recorded from closely spaced minimally pigmented and pigmented areas. A comparison of these spectra showed that the best discrimination between the curves was between 507 nm and 512 nm.

In Fig. 1, a diagram is shown illustrating the correspondence between the coefficient of skin surface reflection and the wavelength of the electromagnetic radiation, to which the skin surface part has been exposed and illustrating a curve A representing the response of an average non-sun-tanned and non-erythrodermic skin surface part of an individual and a curve B representing the response of an erythrodermic or sun-burned skin surface part of an individual. The maximum difference between the curves A and B was between 503 nm and 512 nm for all individuals.

In Fig. 2, a diagram similar to the diagram of Fig. 1 is shown, comprising the curve A also shown in Fig. 1 and further a curve C representing the response of a non-erythrodermic and extremely pigmented skin surface part of an individual. The maximum difference between the curves 30 A and C was between 503 and 512 nm.

In Fig. 3 a diagram is shown, which diagram corresponds to the diagram shown in Fig. 1 in US Patent No. 4.882.598, and which diagram illustrates the linear relationship between the coefficient of reflection to light of a wavelength of 510 nm in logarithmic representation and the time to reach 1 MED using the Solar Simulator recorded for a total of 26 individuals.

On basis of the measuring results illustrated by the curves A, B, and C shown in Figs. 1 and 2, it is concluded that redness influences

the measurements of pigmentation when wavelengths between abt. 380 nm to abt. 600 nm are used. Also the valleys corresponding to the absorption of hemoglobin (abt. 540 - 580 nm) are clearly observed. Reflection within the wavelength area 540 - 580 nm is consequently to be used for estimating redness of the skin and wavelengths above approx. 600 nm and below approx. 380 nm should be used for estimating pigmentation as measurements at these wavelengths are to no substantial extent affected by redness.

Consequently, light sources to be chosen for this purpose are e.g. 10 light-emitting diodes with peak wavelengths at 550 nm (Green) and 660 nm (Red).

A unique measuring probe comprising two light-emitting diodes emitting light of the above wavelengths was designed, which measuring probe is shown in Fig. 5 and is to be discussed in greater detail below.

A further experiment involving 49 volunteers with different pigmentation was made, which experiment revealed relations between the skin surface reflection of red light and green light, which relations constitute the basic realization of the present invention.

In order to investigate in what way redness of the skin influences 20 the estimation of pigmentation, the following test was conducted:

For the above-mentioned 49 individuals green reflection and red reflection were recorded on the antebrachium both on the volar side and on the dorsal side, provided the skin surface of the individual was not too hairy. A total of four situations were tested in one and the same spot ensuring a constant pigmentation. The four situations were: Zero flow, the arm in vertical position, the arm in horizontal position, and a situation in which reactive redness was generated after Zero flow. Zero flow was obtained by pressing all blood out of the arm using elastic bandage followed by obstruction of the blood flow by a cuff on the upper arm. In all cases, the individual was lying in a horizontal position and the skin changes were monitored until the changes had stabilized.

Fig. 6 is a diagram in which the coefficient of skin reflection to red light and the skin reflection to green light in logarithmic representation are listed for all 49 individuals. From the measuring results, it is first of all verified that the coherent sets of skin surface reflection to red light and skin surface reflection to green light in logarithmic representation of the four above listed situations are positioned along straight lines A, B, C, and D, respectively, having a com-

mon intercept at 1.54 at the ordinate axis. The slope of the curve A representing the average Zero flow was deduced from the diagram being 0.03977, and the slope of the straight line D representing the reactive redness situation was also deduced from the diagram being 0.03247. The straight lines B and C representing the vertical and the horizontal position of the arm of the individual, respectively, had slopes in between the slopes of the straight lines A and D. For one and the same individual, the pigmentation should be considered constant in all four situations, and the red reflection should consequently be identical in all 10 four situations. This is, however, not the case. The test revealed that the measurements corresponding to the above described four situations, i.e. corresponding to the straight lines A, B, C, and D, performed on a single individual could be presented by a straight line which, however, was not a vertical line in the diagram shown in Fig. 6. Examples of the 15 signaight line corrections are shown in Fig. 6 which straight lines connect points on the Zero flow line and the corresponding points on the lines B, C, and D corresponding to the above described situations. On the basis of the straight line correction, any set of measuring results representing the skin surface reflection to red and the skin surface re-20 flection to green in logarithmic representation may be, so to speak, normalized as far as redness is concerned by correcting the measuring results to a normalized or standard situation, e.g. a Zero flow situation.

In Fig. 6, a straight dotted line 0 is also shown, representing the average Zero flow plus 2 SD (Standard Deviation) corresponding to a slope of 0.0427, including 95% of the Zero flow measurements. By converting any measuring results representing the skin surface reflection to red and the skin surface reflection to green in logarithmic representation to the straight, dotted line 0, the best possible correction for redness of the skin for calculating the pigmentation may be performed, as will be evident from the discussion below with reference to Fig. 7. An extremely white individual exhibit a skin surface reflection to red of 70% which is consequently named 0% pigmentation, whereas 100% pigmentation corresponds to 0% skin surface reflection to red.

In Fig. 7, redness and pigmentation of a specific individual are calculated on the basis of skin surface reflection measurements to red and green light, the skin surface reflection to green light being presented in logarithmic representation. Thus, Fig. 7 is a diagram, the ab-

scissa and ordinate axes of which are identical to the abscissa and ordinate axes of the diagram shown in Fig. 6. The straight line correction discussed above of the measuring results generated by measuring the coefficients of skin surface reflecction to red and green light of an individual and by converting the green light skin surface reflection coefficient into logarithmic representation is performed along a dotted line C, so to speak transforming the measuring results represented by the point P to a point P' of the line O, i.e. the line intercepting the ordinate at 1.54 and having a slope of 0.0427. The abscissa of the point 10 P' represents the corrected red reflection coefficient and also the pigmentation degree represented in a percentage varying from 0% to 100% as indicated in Fig. 7. Consequently, a specific degree or state of redness for different individuals of different pigmentation is represented by a straight line of constant slope intercepting the ordinate at 1.54. Thus, 15 the degree or state of redness of an individual is readily measurable on the basis of the diagram shown in Fig. 7, as a specific degree or state of redness corresponds to a specific straight line intercepting the ordinate at 1.54 and having a specific slope.

In Fig. 8, a diagram similar to the diagrams shown in Figs. 6 and 7 is shown, representing lines representing different degrees of redness caused by ultraviolet radiation exposed to individuals having different pigmentation. The lines intercept the ordinate axis at 1.54 like the straight lines shown in Figs. 6 and 7. The highest degree of redness corresponding to 100% redness is chosen to include individuals having naevus flammeus of very dark-bluish red colour and corresponds to a straight line of a slope of 0.015.

Table 1 below illustrates the correspondence between clinical redness as defined below, redness percentage and the read-out from an apparatus to be described below with reference to Fig. 4 and implemented in accordance with the teachings of the present invention.

Table 1:

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35	Clinical Redness	Redness %	Display Reading
	0	<29.6	<30
	(+)	32.7	33
	+	37.4	37

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Zero redness corresponds to the highest UV dose of Philips TL12 tubes, which dose may be given before redness appears.

- (+) redness corresponds to faint, spotted redness without a clear demarcation to the surrounding, non-irritated skin surface areas.
- + redness corresponds to faint redness with a clear demarcation to the surrounding skin surface areas.
- ++ redness corresponds to clear redness with slight edema to be felt in the tissue.
  - +++ redness corresponds to heavy redness with edema to be felt or seen above the surrounding skin surface areas.
- The measurements were made after having irradiated the 49 individuals on the buttocks with different doses of UV from Philips TL12 lamps. The doses used were in B-MED (Basic Minimal Erythema Dose being 312 J/m<sup>2</sup> at 296 nm. ((24 h erythema) Parrish). 24 h after irradiation, the redness degree was estimated by means of the above listed "+" system.
- In Fig. 9a, a diagram is shown, illustrating the correspondence between the corrected coefficient of reflection to red and the UV dose in B-MED to reach different levels of erythema. Since all curves exhibit a common intercept at the ordinate axis, a common equation may be deduced which can be used to predict the treatment dose, taking into consideration the degree of pigmentation of the skin surface part in question and further what level of redness is to be produced 24 h after irradiation. The equation used is: Treatment time = 24.2 + (0.1709 x specific redness 5.668) x ln KR (corrected coefficient of reflection to red) x number of seconds to reach a B-MED (the intensity of the light source). The sensitivity of a specific skin surface area of the individual's body relative to the tested part of the buttocks has to be taken into consideration when predicting the treatment dose.

The curves shown in Fig. 9a are almost parallel, and further calculations, according to which calculations the correspondence between the UV dose in B-MED is related to the degree of pigmentation, have proven that dose versus pigmentation may also be used to predict the treatment time. In this case, the additional dose to shift from UV reaction of 0 to +, from + to ++, and from ++ to +++ were identical and independent of

pigmentation (0.69 B-MED). Under these circumstances, the equation is: Treatment time =  $(-0.206 + 0.689 \times \text{ ord. redness (ord. means prescribed)})$ + 0.0829 x pigmentation) x the number of seconds to reach a B-MED (the intensity of the light source).

In Fig. 9b, a diagram is shown, illustrating the correspondence between pigmentation% and the UV-dose in B-MED to reach different levels of erythema. Since all curves are parallel, the curves shown in Fig. 9b are preferably used instead of the curves shown in Fig. 9a, thus substituting the curves shown in Fig. 9a in calculations similar to the 10 above calculations.

The redness "plus" system may be converted into specific figures or numbers as illustrated in Fig. 10, which illustrates the relation between estimated redness and the degree or state of redness in % measured in accordance with the present invention and represented by straight 15 lines.

In Fig. 4 an overall perspective view of an apparatus according to the present invention is shown, which apparatus is designated the reference numeral 10 in its entirety. The apparatus 10 comprises a housing 12 defining a sloping top surface 14 in which a display 16 is arranged 20 together with a 2-digit thumb wheel switch 18 and a 4-digit thumb wheel switch 20. The top surface 14 is further provided with a recess in which a photodetector 40 to be described in greater details below with reference to Fig. 5 is received in the idle mode of the apparatus. The photodetector 40 is connected to the electronic circuitry of the apparatus 25 10 through a multicore cable 42. The apparatus 10 is a mains supplied apparatus and is consequently provided with a mains cable 22 and a mains plug 24. The electronic circuitry of the apparatus 10 is to be described in greater details below with reference to Figs. 11, 12A, 12B, and Example 1.

30 In Fig. 5A, a schematic and partly cut-away view of the photodetector 40 is shown. The photodetector 40 comprises a cylindrical housing 44 in which a printed circuit board 46 is received, which printed circuit board includes the electronic circuitry of the photodetector 40, which electronic circuitry is to be described in greater details below with reference to Fig. 13 and Example 1. The electronic circuitry of the printed circuit board 46 is connected to the multicore cable 42 which extends from the left-hand end of the cylindrical housing 44 through a coiled bushing 48. At the opposite, right-hand end of the cylindrical

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housing 44, a light guide and light-emitting diode supporting and light detector supporting component 50 is received, supported in a fixed position relative to the right-hand end of the photodetector 40 by means of an annular support component 52. In Fig. 5A, a light-emitting diode 54 and a light detector 56 are illustrated received within the component 50 and connected to the printed circuit board 46 through conductors 55 and 57, respectively.

In Figs. 5B and 5C, the component 50 is shown in greater details from the left-hand side and the right-hand side, respectively, relative 10 to the position of the component 50 within the cylindrical housing 44 shown in Fig. 5A. From Figs. 5B and 5C, it is evident that a total of three apertures are provided extending through the component 50 for receiving two light-emitting diodes, one of which emits red light and one of which emits green light, and a light detector. The through-going 15 apertures of the component 50 are designated the reference numerals 60, 62, and 64, respectively. The through-going apertures 60, 62, and 64 are geometrically spaced so as to minimize the risk that any false light may influence the light reflection measurement to be carried out by means of the photodetector 40 in accordance with the teaching of the present in-20 vention and also in accordance with the teaching described in the abovementioned US Patent No. 4.882.598. The apertures 60, 62, and 64 are further arranged in a specific angular and sloping relation so as to obtain an optimum light transmission path from the light-emitting diodes to the light detector from a reflecting surface and further so as to eliminate any light scattering effects from light scattering surfaces, which light scattering might erroneously influence the measurement to be carried out by means of the photodetector 40 and the apparatus 10 according to the present invention, to which apparatus the photodetector 40 is connected.

In Fig. 11, an overall circuit diagram of the electronic circuitry of the apparatus 10 implemented in accordance with the teaching of the present invention is shown. The electronic circuitry is in its entirety designated the reference numeral 100. The electronic circuitry 100 basically comprises the following sections, a mains supply section 102, a photodetector input section 104, an A/D (Analog/Digital) converter sec-35 tion 106, a central microprocessor section or block 108, and an interface section 110 through which interface section, the sections 102, 104, 106, and 108 are connected to one another and further interfaced to the

display 16, the 2-digit thumb wheel switch 18, the 4-digit thumb wheel 20, and a printer output port 112.

The components of the electronic circuitry 100 are listed in the below Example 1.

In Fig. 12, an overall circuit diagram of the microprocessor section or block 108 is shown, which microprocessor block is implemented by an electronic circuit of the type MCS 52, manufactured by the Danish company Circuit Design. The individual components of the microprocessor block or section 108 are listed in the below Example 1.

In Fig. 13, a circuit diagram of the electronic circuitry of the printed circuit board 46 of the photodetector 40 is shown. The individual components of the electronic circuitry 46 are listed in the below Example 1.

## 15 Example 1

The electronic circuitry 100 of the apparatus 10 implemented in accordance with the teaching of the present invention was constructed from the components identified in Fig. 11.

The microprocessor block or section 108 of the electronic circuitry 20 100 was implemented by a circuit of the type MCS-52 supplied by the Danish company Circuit Design. The electronic components of the circuit diagram shown in Fig. 12 were:

	R1	4.7	kohm
25	R2-R4	10	kohm
	R5	47	ohm
	R6	10	kohm
	R7	1	kohm
	R8 ·	10	kohm
30	R9-R11	1	kohm
	R12	10	kohm
	R13	220	ohm
	R14	10	kohm
	R15	1	kohm
35	R16	150	kohm
	R17	10	kohm
	R18	47	kohm
	R19 _	470	kohm

	R20	100 kohm
	R21-R22	10 kohm
	R23	47 ohm
•	R24	4.7 kohm
5	R25-R28	10 kohm
	R29	4.7 kohm
	R30	1 kohm
	C1	100 uF
10	C2-C3	100 nF.
	C4	220 uF
	C5	47 pF
	CC	00
1 5	C6-C9	22 uF
13	C10	100 uF
	C11-C12 C13	22 pF
	C14-C15	22 pF
20	C16-C25	100 nF
	C26-C28 C29	•
	. (29	1 uF
	D1	1N4148
	D2	red LED
25	D3	IN4148
	D4-D6	IN4148
	ΤΙ	BC547
	T2	BC557
30	T3-T4	BC537 BC547
	75 T4	BC557
	T6-T7	BC547
	T8	BC640
	•	500.0
35	ΧI	7.3728 MHz
	X2	32 kHz

LI

150 uH

	ICI	80C31
	IC2	74HC573
	IC3	27064(270256)
5		
	IC4	74HC138
	IC5	74HC133
	- IC6	PAL16L8
10	IC7	74HC573
	IC8	55257 `
	IC9	27C64(27C256)
	IC10	MAX232
15	IC11	MAX630
	IC12	M3002
	IC13	74HC00
	IC14	82C55
	IC15	74HC573
20	IC16	74HC541
	IC17	74HC573
	IC18	74HC541
	IC19	PALI6L8

The photodetector 40 was constructed from the components identified in Fig. 13.

The apparatus according to the present invention fulfilled the below technical specifications:

	Light source	
	LED green	550 nm peak value
	LED red	660 nm peak value
5	Power Requirements	
	Power	220 V
	Dimensions Street	
	Weight	kg
10	Height, length and depth	71×234×272 mm
	Environment	
	Ambient Temperature	17 - 28°C
	Humidity	40 - 80% RH
15		
	Max. variability between	
	measurements under standardized conditions	•
	On brown tile:	·
	Green LED	0,2%
20	Red LED	0,3%
	On white standards:	
*	Green LED	0,3%
	Red LED	0,6%
	Max. interapparatus variability	+/- 2,5% on skin
25	Measuring time (from 1st to last beep)	-4,5 sec

#### Example 2

The microprocessor of the microprocessor section or block 108 of the apparatus according to the present invention was operated by means of the programme listed in Table 2 or alternatively operated by means of the programme listed in Table 3. This programme is working in the same way as the programme listed in Table 2 but is giving a warning when the patient is read instead of recalculation of the dose. That allows the operator or the doctor to decide if any reduction in treatment time should be performed.

Provided the 2-digit thumb wheel is set to 15, the number of joules/sqcm will be calculated for PUVA-treatment (- 300 + 2200 x ord.

 $\mathcal{H}$ 

redness (ord. means prescribed) + 205 x pigment%). This dose should come from a Philips TL 09 lamp or a lamp with a similar spectral distribution. Likewise, it is possible to have the treatment dose in joule or m joules/sqcm for different lamp types when the thumb wheel to the left in Fig. 4 is set to 1-13. 14 is the code used when only pigment protection factor, skin redness, and skin pigmentation is to be shown on the display.

1.

#### Table 2:

```
10
       REM 25.1.1992 PRG2.BAS
20
       REM 100% refl=900 mV
30
       REM FFE7H=65511=CONTROLREG.
40
       REM FFE6H=65510= C-PORTE
50
       REM FFE5H=65509= B-PORTE.
60
       REM FFE4H=65508= A-PORTE.
70
       BAUD 2400 : REM BAUDRATE TIL DISPLAY
80
      XBY(65511)=145 : REM A INPUT,B OUTPUT,C-LOW INPUT,C-HI OTPUT
90
       GDSUB 2010
100
       G0SUB 2030
110
       FRINT #"
120
      JUMPER=XBY(65508).AND.128 : IF JUMPER=0 THEN 2140
130
       FOR P=0 TO 5
140
      XBY(65509)=2**P
150
      SW(F)=XBY(65510).AND.15
160
      NEXT P
      SW2=1000*SW(3)+100*SW(2)+10*SW(1)+SW(0) : REM S/MED FOR KILDEN
170
180
      SW1=10*SW(5)+SW(4)
      ORD=SW1*.1 : REM ORDINERET 24H ROD (1 DECIMAL:
185
      .IF SW2=0 THEN 1630
190
200
      XBY(65510)=0 : REM DIODES OFF
210
      F=0 : SB=0
220
      N≃Θ
230
       GOSUB 640
240
       IF M(N)>100 THEN 130
250
       IF SW1>30 THEN 300
590
       GDSUB 2010
       EDSUB 2030
270
280
       PRINT #"
290
       GOTO 340
300
       GDSUB 2010
310
       GOSUB 2050
320
       FRINT #"
330
       GOTO 130
340
      N=N+1
350
       IF NK3 THEN 230
      XBY(65509)=128 : REM PB7=LYDGIVER ON FOR T=0 TO 10 : NEXT T
360
370
380
      XBY(65509)=0 : REM PB7=LYDGIVER OFF
390
      XBY(65510)=16 : REM PC4 HI GREEN DIODE ON.
400
       FOR T=0 TD 200 : NEXT T
410
       FOR N=0 TO 4
420
       GOSUB 640
430
      G(N)=M(N)
440
       NEXT N
450
      XBY(65509)=128
460
       FOR T=0 TO 10 : NEXT T
470
      XBY(65509)=0
480
      XBY(65510)=0: REM DIODES OFF
490
       FOR T=0 TO 200 : NEXT T
500
       FOR N=0 TO 4
510
       GDSUB 640
520
      S(N)=M(N)
530
       NEXT N
540
      XBY(65509)=120
550
       FOR T=0 TO 10 : NEXT T
```

```
560
      XBY(65509)=0
      XBY(65510)=64 : REM FC6 HI RED : 10DE ON.
570
      FOR T=0 TO 200 : NEXT T
580
      FOR N=0 TO 4
590
      GOSUB 640
600
      R(N)=M(N)
610
       NEXT N
620
       GOTO 830
630
640
       DO
      I=XBY(65508) : C=I.AND.112
650
       UNTIL C=112 : REM I.E.PA6,PA5 OG PA4 HI.
660
670
      I=XBY(65508): C=I.AND.112
686
       UNTIL C=48: REM I.E. PA6 LO I.E. HUNDREDS SELECTED.
490
700
      H=I.AND.15
710
720
      I=XBY(65508) : C=I.AND.112
        UNTIL C=96 : REM I.E. PA4 LO I.E. UNITS SELECTED.
730
      U=I.AND.15
740
750
       I=XBY(65508) : C=I.AND.112
760
        UNTIL C=80 : REM I.E. PAS L I.E. TENS SELECTED.
 770
780
       T=I.AND.15
 790
      FT=1
       IF H=10 THEN H=0 : FT=-1
800
       M(N)=FT*(100*H+10*T+U)
 810
       RETURN
 820
       XBY(65509)=128 : XBY(65510)=0
 830
       FOR T=0 TO 100 : NEXT T
 840
       XBY(65509)=0
 850
       GMIN=1000 : SMIN=1000 : RMIN=1000
 960
       GMAX=0 : SMAX=0 : RMAX=0
 870
       GS=0 : SS=0 : RS=0
 889
 899
       FOR N=0 TO 4
       GS=GS+G(N) : SS=SS+S(N) : RS=RS+R(N)
 900
        IF G(N)<GMIN THEN GMIN=G(N)
 910
        IF G(N)>GMAX THEN GMAX=G(N)
 920
        IF S(N) < SMIN THEN SMIN=S(N)
 930
        IF S(N)>SMAX THEN SMAX=S(N)
 740
 950
        IF R(N) < RMIN THEN RMIN=R(N)
        IF R(N)>RMAX THEN RMAX=R(N)
 960
 970
         NEXT N
         IF GMAX-GMIN>40 THEN F=1
 980
         IF SMAX-SMIN>10 THEN F=1
 990
         IF RMAX-RMIN>40 THEN F=1
 1000
  1010 FG=.1*INT((GS-SS)/4.5)
  1020 RR=.1*INT((RS-SS)/4.5)
         IF RGK5 THEN F=1
  1030
         IF F=1 THEN 1180
  1050
        GI=LOG(RG)-1.54 : REM ln(RG)-intercept
  1100
  1110 SL=GI/RR : REM slope
  1120 KR=RR+17.5*(1-SL/.0427) : REM KORR. RED REFL.
  1130 KGI=.0427*KR : REM KORR GR REFL
        IF KR=0 THEN F=1
  1150
        IF KR<0 THEN F=1
  1160
```

IF F=0 THEN 1350

1170

)

£11.7%

```
1180
       GOSUB 2010
1170
       GOSUB 2070
1200
       GDSUB 2090
1210
       FOR T=0 TO 600 : NEXT T
1220
       GOTO 90
      PMT=100*(70-KR)/70 : IF PMT<0 THEN PMT=0
1350
      REDN=100*(.0427-SL)/.0277 : IF REDN<0 THEN REDN=0
1360
1365
       IF PMT>60 THEN SB=1
1370
      PMT=INT(PMT)
1380
      REDN=INT (REDN)
       PRINT #CHR(27),"I",CHR(17),CHR(22),
1370
       PRINT #" PIGMENTATION ",PMT,"%"
1400
       IF SB=1 THEN PRINT #" REDNESS UNRELIABLE " : 60TO 1480
1405
       PRINT #" REDNESS
1410
                             ",FEDN,"%"
       FOR T=0 TO 1500 : NEXT T
1420
1430 PP=24.2-5.4971*LOG(KR): REM PIGM.BESK.FAKTOR
      PP=.1*INT(10*PP)
      PRINT #CHR(27), "I", CHR(17), CHR(22),
1450
       PRINT #" PIGMENT PROTECTION"
1460
1465
       IF PP>.5 THEN 1470
1467
       PRINT #"
                    UNRELIABLE
1468
       FOR T=0 TO 1500 : NEXT T
1469
       GOTO 90
1470
       PRINT #" FACTOR ",PP
       FOR T=0 TO 1500 : NEXT
1480
      ARD=16.97-491.5*SL : REM ACTUELL REDNESS
1485
1487
       IF PMT>60 THEN 1500
1490
       IF REDN>29.6 THEN 1510
      TT=.5*(24.2+(.1709*ORD-5.668)*LOG(KR))*SW2 : GOTO 1520
1500
1510
      TT=.1709*(ORD-ARD)*LOG(KR)*SW2
      PRINT #CHR(27),"I",CHR(17),CHR(22),
1520
      TT=INT(TT) : IF TT(0 THEN TT=0
1530
1549
      H=INT(TT/3600)
1550
      M=INT((TT-3600*H)/60)
1560
      S=TT-M*60-H*3600
1570
       PRINT #"
               TREATMENT TIME "
1580
       IF H=0 THEN 1600
       PRINT #" ",H,"HOUR",M,"MIN" : GOTO 1622
1590
       IF M=0 THEN 1620
1600
       PRINT #" ",M,"MIN ",S,"SEC ": GOTO 1622
1610
1620
       PRINT #"
                   ",S,"SEC
                              " : GOTO 1622.
1622
       FOR T=0 TO 1500 : NEXT T
1624
       60TO 120
       PRINT #CHR(27), "I", CHR(17), CHR(22),
1630
1649.
       PRINT #"*CALIBRATE*
                             PLACE"
      PRINT #"DETECTOR ON STANDARD"
1650
1669
      XBY(65509)=1
     SW=XBY(65510).AND.15 : IF SW>0 THEN 10
1670
1680
     XBY(65509)=2
     SW=XBY(65510).AND.15 : IF SW>0 THEN 10
1699
1700
     XBY(65509)=4
1710
     SW=XBY(65510).AND.15 : IF SW>0 THEN 10
1720
      XBY(65509)=8
1730
     SW=XBY(65510).AND.15 : IF SW>0 THEN 10
1749
      FOR T=0 TO 1000 : NEXT T
1750 XBY(65510)=32
```

```
FOR T=0 TO 200 : NEXT T
1760
1770
       G0SUB 640
1780
      S=M(N)
1790
       IF S>40 THEN 1630
1800
      XBY(65510)=48
1810
       FOR T=0 TO 200 : NEXT T
1820
       GOSUB 640
1830
      G=M(N)
1840
      GP=.1*INT((G-S)/.9)
1850
      XBY(65509)=128
1869
       FOR T=0 TO 5 : NEXT T
1870
      XBY(65509)=0
       PRINT #CHR(27),"I",CHR(17),CHR(22),
1886
       PRINT #GP,"%", TAB (9), "GREEN
1890
1900
      XBY(65510)=96
1910
       FOR T=0 TO 200 : NEXT T
1920
       GOSUB 640
1930
      R=M(N)
1740
      XBY(65510)=32
1750
      RP=.1*INT((R-S)/.9)
1960
      XBY(65509)=128
1970
       FOR T=0 TO 15 : NEXT T
1980
      XBY(65509)=0
1990
       PRINT #RP, "%", TAB (5), "RED
2000
       GOTO 1660
       PRINT #CHR(27), "I", CHR(17), CHR(22),
2010
2020
       RETURN
2030
       PRINT #"
                  *** READY ***
2040
       RETURN
2050
      PRINT #" CHECK DOSE SETTING"
2060
       RETURN
      PRINT #"ERROR ERROR ERROR"
2070
2080
       RETURN
2090
      PRINT #" REPEAT MEASUREMENT"
2100
       RETURN
2110
       REM ***
2120
       REM ***
2130
       REM ***
      REM TESTPG FOR HUDREFLEKTANSMETER.TEST.BAS
2140
2150
       REM *** INITIALISERING
2160
      REM 100% ref1=900 mV
      REM FFE7H=65511=CONTROLREG.
2170
2180
      REM FFE6H=65510= C-PORTE
2190
      REM FFE5H=65509= B-PORTE.
2200
      REM FFE4H=65508= A-PORTE.
2210
      BAUD 2400 : REM BAUDRATE TIL DISPLAY
2220
     XBY(65511)=145 : REM A INPUT,B OUTPUT,C-LOW INPUT,C-HI OUTPUT
      PRINT #CHR(27), "I", CHR(17), CHR(22),
2230
2240
      REM *** INIT SLUT
2250
      PRINT #"TESTER LYDGIVER"
2269
      FOR N=0 TO 1
2270
      XBY(65509)=128
2280
      FOR T=0 TO 50 :
                        NEXT T
2290
     XBY(65509)=0
2300
      FOR T=0 TO 50 :
                       NEXT T
2310
      NEXT N
```

```
PRINT #" TESTER OMSKIFTERE"
2320
2330
      DIM SW(6)
2340
      FOR P≃0 TO 5
2350 XBY(65509)=2**P
2360
     SW(P)=XBY(65510).AND.15
2370
     NEXT P
2380
      FOR P=5 TO 4 STEP -1
2390
      PRINT #SW(P),
2400
      NEXT P
2410
      PRINT #" ",
      FOR P=3 TO 0 STEP -1
2420
2430
     PRINT #SW(P),
2440
      NEXT P
2450
     PRINT #
2460
      SW2=1000*SW(3)+100*SW(2)+10*SW(1)+SW(0)
2470
      SW1=10*SW(5)+SW(4)
2480
      IF SW2=0 THEN 2500
2490
       GOTO 2340
2500
      PRINT #CHR(27), "I", CHR(17), CHR(22),
       PRINT #" A/D-CONV.UDG. mV"
2510
2520
       GOSUB 2750
2530
       PRINT #" ",M, TAB (10),"
2540
      FRINT #""
2550
     XBY(65509)=1 : SW(0)=XBY(65510).AND.15
2560
      IF SW(0)=1 THEN 2600
2570
       IF SW(0)=2 THEN 2670
       GOTO 2520
2580
2590
      GOTO 2520
2600 XBY(65510)=16 : REM PC4 HI GREEN DIODE ON.
2610
      FOR T=0 TO 200 : NEXT T
2620
       GDSUB 2750
5630
      XBY(65510)=0: REM DIODES OFF
       PRINT #" ",M, TAB (10), "GREEN
2640
2650
       PRINT #""
2660
       GOTO 2550
2670 XBY(65510)=64 : REM PC6 HI RED DIODE ON
2680
      FOR T=0 TO 200 : NEXT T
       GOSUB 2750
2690
2700 XBY(65510)=0 : REM
                            DIODES OFF
       PRINT #" ",M, TAB (10), "RED
2710
2720
       PRINT #""
2730
       GOTO 2550
2740
       REM ***AFLAESNING AD A/D-CONVERTER
2750
      I=XBY(65508) : C=I.AND.112
      UNTIL C=112 : REM I.E.PA6,PA5 OG PA4 HI.
2770
2780
2790
      I=XBY(65508) : C=I.AND.112
      UNTIL C=48 : REM I.E. PA6 LO I.E. HUNDREDS SELECTED.
2800
2810
      H=I.AND.15
5850
      DO
2830 I=XBY(65508) : C=I.AND.112
      UNTIL C=96 : REM I.E. PA4 LO I.E. UNITS SELECTED.
2840
2850 U=I.AND.15
5840
      DO
2870 I=XBY(65508) : C=I.AND.112
```

```
2880 UNTIL C=80 : REM I.E. PA5 L I.E. TENS SELECTED.
2890 T=I.AND.15
2900 FT=1
2910 IF H=10 THEN H=0 : FT=-1
2920 M=FT*(100*H+10*T+U)
2930 RETURN
```

REM \*\*\* AFLAESNING SLUT

```
Table 3:
        REM 18.1.1993 PRG2.BAS MOD TIL SPEC3.BAS
 10
 20
        REM 100% ref1=900 mV
 30
        REM FFE7H=65511=CONTROLREG.
 40
        REM FFE6H=65510= C-PORTE
 50
        REM FFE5H=65509= B-PORTE.
 60
       REM FFE4H=65508= A-PORTE.
 70 -
        BAUD 2400 : REM BAUDRATE TIL DISPLAY
 80 .
       XBY(65511)=145 : REM A INPUT, B OUTPUT, C-LOW INPUT, C-HI OUTPUT
 90
        GOSUB 2010
 100
        GOSUB 2030
 110
        PRINT #"
 120
       JUMPER=XBY(65508).AND.128 : IF JUMPER=0 THEN 2140
 130
       FOR P=0 TO 5
 140
       XEY(65509) = 2 \times P
 150
       SW(P) = XBY(65510).AND.15
 160
 170
       SW2=1000*SW(3)+100*SW(2)+10*SW(1)+SW(0) : REM S/MED FOR KILDEN
       SW1=10*SW(5)+SW(4)
 180
       ORD=SW1*.1 : REM ORDINERET 24H ROD (1 DECIMAL)
 185
 190
       IF SW2=0 THEN 1630
 200
       XBY(65510)=0 : REM DIODES OFF
 210
       F=0 : SB=0
 2.20
       N=0
 230
        GOSUB 640
 240
      IF M(N)>100 THEN 130
 250
        IF SW1>40 THEN 300
 260
        GOSUB 2010
 270
        GOSUB 2030
 280
        PRINT #"
 290
        GOTO 340
 300
        GOSUB 2010
 310
        GOSUB 2050
 320
        PRINT #"
 330
        GOTO 130
 340
       N=N+1
 350
        IF N<3 THEN 230
       XBY(65509)=128: REM PB7=LYDGIVER ON FOR T=0 TO 10 : NEXT T
 360
 370
 380
       XBY(65509)=0 : REM PB7=LYDGIVER OFF
       XBY(65510)=16: REM PC4 HI GREEN DIODE ON.
FOR T=0 TO 200: NEXT T
390
 400
 410
        FOR N=0 TO 4
 420
        GOSUB 640
 430
       G(N)=M(N)
 440
        NEXT N
 450
       XBY(65509)=128
 460
        FOR T=0 TO 10 : NEXT T
 470
       XBY(65509)=0
 480
       XBY(65510)=0 : REM DIODES OFF
 490
        FOR T=0 TO 200 : NEXT T
 500
         FOR N=0 TO 4
 510
        GOSUB 640
 520
       S(N)=M(N)
 530
        NEXT N
 540
       XBY(65509)=128
 550
        FOR T=0 TO 10 : NEXT T
```

```
560
     XBY(65509)=0
570
     XBY(65510)=64: REM PC6 HI RED DIODE ON.
580
       FOR T=0 TO 200 : NEXT T
590
       FOR N=0 TO 4
       GOSUB 640
600
610
      R(N) = M(N)
620
       NEXT N
630
       GOTO 830
640
650
      I=XBY(65508) : C=I.AND.112
660
       UNTIL C=112 : REM I.E.PA6,PA5 OG PA4 HI.
670
680
      I=XBY(65508) : C=I.AND.112
690
       UNTIL C=48: REM I.E. PA6 LO I.E. HUNDREDS SELECTED.
700
      H=I.AND.15
710
720
      I=XBY(65508) : C=I.AND.112
       UNTIL C=96 : REM I.E. PA4 LO I.E. UNITS SELECTED.
730
740
      U=I.AND.15
750
760
      I=XBY(65508) : C=I.AND.112
       UNTIL C=80 : REM I.E. PA5 L I.E. TENS SELECTED.
770
780
      T=I.AND.15
790
800
       IF H=10 THEN H=0 : FT=-1
810
      M(N) = FT * (100 * H + 10 * T + U)
820
      RETURN
      XBY(65509)=128 : XBY(65510)=0
830
840
       FOR T=0 TO 100 : NEXT T
850
      XBY(65509)=0
860
      GMIN=1000 : SMIN=1000 : RMIN=1000
      GMAX=0 : SMAX=0 : RMAX=0
870
880
      GS=0 : SS=0 : RS=0
890
      FOR N=0 TO 4
 900
      GS=GS+G(N) : SS=SS+S(N) : RS=RS+R(N)
 910
       IF G(N) < GMIN THEN GMIN=G(N)
 920
       IF G(N)>GMAX THEN GMAX=G(N)
 930
       IF S(N) < SMIN THEN SMIN=S(N)
 940
       IF S(N)>SMAX THEN SMAX=S(N)
 950
        IF R(N) < RMIN THEN RMIN=R(N)
 960
        IF R(N)>RMAX THEN RMAX=R(N)
 970
        NEXT N
 980
        IF GMAX-GMIN>40 THEN F=1
 990
        IF SMAX-SMIN>10 THEN F=1
       IF RMAX-RMIN>40 THEN F=1
 1000
 1010 RG=.1*INT((GS-SS)/4.5)
 1020 RR=. I*INT((RS-SS)/4.5)
       IF RG<5 THEN F=1
 1030
        IF F=1 THEN 1180
 1050
 1100 GI=LOG(RG)-1.54: REM ln(RG)-intercept
 1110 SL=GI/RR : REM slope
 1120 KR=RR+17.5*(1-SL/.0427) : REM KORR. RED REFL.
 1130 KGI=.0427*KR : REM KORR GR REFL
 1150
        IF KR=0 THEN F=1
 1160
        IF KR<0 THEN F=1
 1170
        IF F=0 THEN 1350
```

```
1180
       GOSUB 2010
 1190
       GOSUB 2070
 1200
       GOSUB 2090
 1210
       FOR T=0 TO 600 : NEXT T
1220
       GOTO 90
1350 PMT=100*(70-KR)/70 : IF PMT<0 THEN PMT=0
1360 REDN=100*(.0427-SL)/.0277 : IF REDN<0 THEN REDN=0
 1365
       IF PMT>60 THEN SB=1
1370
      PMT=INT(PMT)
 1380 REDN=INT(REDN)
      PRINT #CHR(27), "I", CHR(17), CHR(22),
 1390
 1400
       PRINT #" PIGMENTATION ", PMT, "%"
       IF SB=1 THEN PRINT #" REDNESS UNRELIABLE " : GOTO 1420
 1405
       PRINT #" REDNESS ", REDN, "%"
1410
       FOR T=0 TO 2000 : NEXT T
1420
      PP=.483+.0829*PMT : REM PIGM.BESK.FAKTOR
1430
1440 PP=.1*INT(10*PP)
1450
       PRINT #CHR(27); "I", CHR(17), CHR(22),
1460
       PRINT #" PIGMENT PROTECTION"
 1465
       IF PP>.483 THEN 1470 : REM IF PMT=0
1467
       PRINT #" UNRELIABLE
1468
       FOR T=0 TO 2000 : NEXT T
1469
       GOTO 90
1470
       PRINT #" FACTOR ", PP
1480
       FOR T=0 TO 2000 : NEXT
1485 ARD=16.97-491.5*SL : REM ACTUELL REDNESS
1486
       IF PMT<13 THEN PMT=13 : REM TAALES ALTID
1488
       IF SW2>0.AND.SW2<16 THEN GOTO 3000
1490
       IF PMT>60 THEN 1500
       REM IF REDN>29.6 THEN 1510 erstattet af advarsei
1491
1492
       IF REDN<29.6 THEN 1500
1493
       PRINT #CHR(27), "I", CHR(17), CHR(22),
1494
       FOR T=O TO 4
1495
       PRINT #" CHECK SKIN REDNESS "
1496
       FOR P=0 TO 200 : NEXT P
1497
       PRINT #"
1498
       FOR P=0 TO 50 : NEXT P
1499
       NEXT T
1500
      TT=(-0.9+.689*ORD+.0829*PMT)*SW2
1502
       IF SW15=1 THEN TT=-2300+2200*ORD+205*PMT : SW15=0
1503
       REM -2000 PGA REGIONSFORSKELLE.
1506
       GOTO 1520
1510
       REM TT=.689*(ORD-ARD)*SW2
1520 PRINT #CHR(27), "I", CHR(17), CHR(22),
1530 TT=INT(TT): IF TT<0 THEN TT=0
1531
       IF LSW=0 THEN 1540
1532
       PRINT #"
                 TREATMENT DOSE "
1533
      IF TT<1000 THEN PRINT #"
                                   ",TT, "MJ/SQCM" : GOTO 1537
1534
      TT=INT(TT/100) : UVD=TT/10
1536
       PRINT #" ",UVD, "J/SQCM"
1537
       FOR T=0 TO 2000 : NEXT T
1538
      LSW=0
1539
       GOTO 120
1540 H=INT(TT/3600)
1550 M=INT((TT-3600*H)/60)
1560 S=TT-M*60-H*3600
```

```
1570
       PRINT #"
                 TREATMENT TIME "
1580
       IF H=0 THEN 1600
       PRINT #" ",H,"HOUR",M,"MIN" : GOTO 1622
1590
       IF M=0 THEN 1620
1600
       PRINT #" ",M,"MIN ",S,"SEC " : GOTO 1622
1610
                  ";S,"SEC " : GOTO 1622
       PRINT #"
1620
1622
       FOR T=0 TO 2000 : NEXT T
1624
       GOTO 120
1630
       PRINT #CHR(27), "I", CHR(17), CHR(22),
1640
       PRINT #"*CALIBRATE*
                             PLACE"
1650
       PRINT #"DETECTOR ON STANDARD"
1660
      XBY(65509)=1
1670
      SW=XBY(65510).AND.15 : IF SW>0 THEN 10
1680
      XBY(65509)=2
1690
      SW=XBY(65510).AND.15 : IF SW>0 THEN 10
1700
      XBY(65509)=4
1710
      SW=XBY(65510).AND.15 : IF SW>0 THEN 10
1720
      XBY(65509) = 8
1730
      SW=XBY(65510).AND.15 : IF SW>0 THEN 10
1740
      FOR T=0 TO 1000 : NEXT T
1750
      XBY(65510)=32
1760
       FOR T=0 TO 200 : NEXT T
1770
       GOSUB 640
1780 S=M(N)
1790 IF S>40 THEN 1630
1800
      XBY(65510)=48
       FOR T=0 TO 200 : NEXT T
1810
1820
       GOSUB 640
1830
      G=M(N)
1840
      GP=.1*INT((G-S)/.9)
1850
      XBY(65509)=128
1860
      FOR T=0 TO 5 : NEXT T
1870
      XBY(65509)=0
       PRINT #CHR(27), "I", CHR(17), CHR(22),
1880
1890
       PRINT #GP, "%", TAB (9), "GREEN
1900
      XBY(65510) = 96
1910
       FOR T=0 TO 200 : NEXT T
1920
       GOSUB 640
1930
      R=M(N)
1940
      XBY(65510)=32
1950
      RP = .1 \times INT((R-S)/.9)
1960
      XBY(65509)=128
1970
       FOR T=0 TO 15 : NEXT T
1980
      XBY(65509)=0
       PRINT #RP, "%", TAB (9), "RED
1990
2000
        GOTO 1660
2010
       PRINT #CHR(27), "I", CHR(17), CHR(22),
2020
        RETURN
2030
        PRINT #"
                   *** READY ***
2040
        RETURN
2050
        PRINT #" CHECK DOSE SETTING"
2060
        RETURN
2070
        PRINT #"ERROR ERROR ERROR"
2080
        RETURN
2090
        PRINT #" REPEAT MEASUREMENT"
2100
        RETURN
```

```
2110
     REM ***
2120
     REM ***
2130
      REM ***
2140
      REM TESTPG FOR HUDREFLEKTANSMETER. TEST. BAS
2150
      REM *** INITIALISERING
2160
     REM 100% ref1=900 mV
2170
      REM FFE7H=65511=CONTROLREG.
2180
      REM FFE6H=65510= C-PORTE
2190
      REM FFE5H=65509= B-PORTE.
2200
      REM FFE4H=65508= A-PORTE.
2210
      BAUD 2400 : REM BAUDRATE TIL DISPLAY
2220 XBY(65511)=145 : REM A INPUT, B OUTPUT, C-LOW INPUT, C-HI OUTPUT
2230
      PRINT #CHR(27), "I", CHR(17), CHR(22),
2240
      REM *** INIT SLUT
2.250
      PRINT #"TESTER LYDGIVER"
2260
      FOR N=0 TO 1
2270 XBY(65509)=128
2280
      FOR T=0 TO 50 : NEXT T
2290: XBY(65509)=0
2300
     FOR T=0 TO 50 : NEXT T
2310
     NEXT N
      PRINT #" TESTER OMSKIFTERE"
2320
2330
     DIM SW(6)
2340
     FOR P=0 TO 5
2350 XBY(65509)=2**P
2360 SW(P)=XBY(65510).AND.15
2370
     NEXT P
2380
     FOR P=5 TO 4 STEP -1
      PRINT #SW(P),
2390
2400
     NEXT P
      PRINT #" "
2410
      FOR P=3 TO 0 STEP -1
2420
2430
     PRINT #SW(P).
2440 NEXT P
2450
      PRINT #
2460 SW2=1000*SW(3)+100*SW(2)+10*SW(1)+SW(0)
2470 \text{ SW1}=10 \times \text{SW}(5) + \text{SW}(4)
      IF SW2=0 THEN 2500
2480
2490
      GOTO 2340
      PRINT #CHR(27), "I", CHR(17), CHR(22),
2500
2510
      PRINT #" A/D-CONV.UDG. mV"
2520
       GOSUB 2750
2530
      PRINT #" ",M, TAB (10),"
2540
      PRINT #""
2550 XBY(65509)=1 : SW(0)=XBY(65510).AND.15
2560
      IF SW(0) = 1 THEN 2600
      IF SW(0) = 2 THEN 2670
2570
2580
      GOTO 2520
2590
      GOTO 2520
2600 XBY(65510)=16 : REM PC4 HI GREEN DIODE ON.
2610
      FOR T=0 TO 200 : NEXT T
2620
      GOSUB 2750
2630 XBY(65510)=0 : REM DIODES OFF
2640
      PRINT #" ",M, TAB (10), "GREEN
       PRINT #""
2650
2660
       GOTO 2550
```

```
2670 XBY(65510)=64 : REM PC6 HI RED DIODE ON
2680
      FOR T=0 TO 200 : NEXT T
2690
      GOSUB 2750
2700
     XBY(65510)=0 : REM
                           DIODES OFF
2710
      PRINT #" ",M, TAB (10), "RED
      PRINT #""
2720
273C
      GOTO 2550
      REM ***AFLAESNING AD A/D-CONVERTER
2740
2750
      DO
                                                  ·-:
2760
     I=XBY(65508) : C=I.AND.112
2770
     UNTIL C=112 : REM I.E.PA6,PA5 OG PA4 HI.
2780
2790
     I=XBY(65508) : C=I.AND.112
      UNTIL C=48 : REM I.E. PA6 LO I.E. HUNDREDS SELECTED.
2800
2810
     H=I.AND.15
2820
2830
     I=XBY(65508) : C=I.AND.112
      UNTIL C=96 : REM I.E. PA4 LO I.E. UNITS SELECTED.
2840
2850 U=I.AND.15
2860
      DO
     I=XBY(65508) : C=I.AND.112
2870
      UNTIL C=80 : REM I.E. PA5 L I.E. TENS SELECTED.
2880
2890
     T=I.AND.15
2900
     FT=1
2910
      IF H=10 THEN H=0 : FT=-1
2920
     M=FT*(100*H+10*T+U)
2930
       RETURN
       REM *** AFLAESNING SLUT
2940
3000
     LSW=1
       IF SW2=1 THEN SW2=334 : REM INCL CORR 1.85
3010
       IF SW2=2 THEN GOTO 3200
3020
       IF SW2=3 THEN GOTO 3200
3030
      IF SW2=4 THEN GOTO 3200
3040
       IF SW2=5 THEN GOTO 3200
 3050
       IF SW2=6 THEN GOTO 3200
 3060
 3070 · IF SW2=7 THEN GOTO 3200
       IF SW2=8 THEN SW2=52880
 3080
       IF SW2=9 THEN SW2=21081
 3090
 3100
       IF SW2=10 THEN SW2=52880
 3110
       IF SW2=11 THEN GOTO 3200
       IF SW2=12 THEN SW2=82
 3120
       IF SW2=13 THEN GOTO 3200
 3130
 3140
       IF SW2=14 THEN goto 120
       IF SW2=15 THEN SW15=1
 3150
 3160
        GOTO 1490
 3200
        GOSUB 2010
 3210
        GOSUB 2070
        FOR T=0 TO 2000 : NEXT T
 3220
 3230
        GOTO 90
```

In case the programme is adapted to control the microprocessor of the apparatus according to the present invention in accordance with the above described alternative calculations relating to the comparison of the UV dose in B-MED and the degree of pigmentation, the lines 1500 and 1510 of the programme are amended into:

TT=(-0.206+0.689xORD+0.0829xPIG%) and TT=.689x(ORD-ARD).

The apparatus according to the present invention should be operated 10 in accordance with the below measuring guidelines:

The undressed patient should acclimate before the measurement. This is to evaporate sweat from the skin and cool. Measurements is performed on normal or relatively normal skin avoiding discoloration from treatment, freckles, hairy areas even after shaving, flushing zones, and skin irritated from rubbing by the person himself or from the back of a chair. If fullbody treatment is performed the best place to measure is on the back above a horizontal line through the lower part of the scapulae, and on the upper part of the abdomen and the breast. Measurements on the extremities will only be reproducible if the patient is placed horizontally and relaxing. Redness will change with level and activity.

The detector is held perpendicular to the surface of the skin gently touching the skin in order to eliminate light from entering the detector from the environment.

Light sources used for the treatment of skin diseases may have very different biological activity. And since the limiting factor for the treatment dose is redness of the skin, the use of a basic MED has been chosen as the basic dose. The basic MED being calculated from the erythema action spectrum CIE (McKinlay & Diffey) and the MED dose of 31,2 mJ/cm2 at 296 nm (Parrish).

The correct number of seconds to reach that dose, i.e. 1B-MED, is entered into the microprocessor by means of the the thumb wheel 20 at the right-hand side of the display 16.

By means of the thumb wheel 16 at the left-hand side of the display 20, the "24h erythema level" is input. This level has to be decided by the person operating the apparatus.

0.0 Corresponds to the highest dose which can be given before redness will appear.

- 0.5 Corresponds to (+) redness, weak spotted redness without sharp borders to the untreated surroundings.
- 5 1.0 Weak redness with a clear demarcation to the surroundings. Often named +.
  - 2.0 Corresponds to redness ++ with clear redness and a weak edema to be felt.

3.0 Corresponds to +++ redness. There is heavy redness with edema above the surroundings.

Therefore, the following schedule is recommended for the treatment 15 of psoriasis:

	<ol> <li>Week of treatment</li> </ol>	setting 1.0
•	<ol><li>Week of treatment</li></ol>	3.0
	3. week of treatment	6.0
20	4. Week of treatment	9.0

A constant erythema level setting may be used for atopic dermatitis mycosis fungiodes, pruritus etc.

#### 25 Pigmentation

The scale has been chosen so that people with a very wide range of pigmentation covering all races are represented in the scale. Pigmentation is given on a scale from 0% to 100%. 0% pigmentation represents the degree of pigmentation of previously unirradiated buttocks of an extremely white person. 100% pigmentation represents the degree of pigmentation of previously unirradiated buttocks of a very black person.

In the first few days after intensive UV irradiation redness corresponding to ++ and +++ etc. will result in a lower measure of pigmentation than the measurement preceding irradiation. This phenomenon is a result of edema following heavy erythema and is caused by erythema itself.

1

Erythema

The scale is chosen so that people with zero blood flow and dark blue red naevus flammeus can be fitted into the scale.

O% redness has been chosen as the redness of the skin on the antebrachium of persons who had their arm emptied for blood and the blood supply stopped by a cuff on the upper arm.

100% has been chosen so that even very blue-red naevus flammeus of the face may be included.

10 0-30% corresponds to what is found under normal conditions in connection with people acclimated to room temperature.

The relations between the clinical degree of redness and the average % of UV irradiated people or individuals are listed in Table 1.

The pigment protection factor indicates how much higher UV dose an individual can take before obtaining + in redness compared to a person reacting with + redness.

After exposure to 1 B-MED from a Philips TL 12 equipped radiation source. All background measurements are to be performed on previously unexposed buttocks.

Treatment time shown on the display 16 is the time used for full body irradiation. Therefore, the irradiation dose matches the most sensitive larger areas of the body. It should be noted that the treatment time depends on the radiation source and the setting of the thumb wheel switch 20.

When the thumb wheel switch 20 at the right-hand side of the display 16 is adjusted to 0000 (no radiation) the apparatus automatically jumps into calibration mode.

Keeping the detector close to the tile which is delivered together with the apparatus a reflection % for the red and green light is shown on the display. This reflection should be within the limits written on the tile.

Before calibration, the apparatus must be in temperature equilibrium with the room in which the apparatus is to be used.

The calibration values is traceable to standard ISO 2469. Using 35 this standard will display 100% both for red and green reflection.

The detector is constructed to demand a minimum of cleaning. Only a plastic ring is in contact with the skin. This may be cleaned by an alcoholic solution.

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In Fig. 14 a diagram is shown illustrating the basic realization that a linear relationship exists between light- or laser-induced skin changes to individuals and the degree of skin pigmentation of the same individuals. The diagram shown in Fig. 14 was based on the below test.

Thirteen individuals with a varying degree of epidermal skin pigmentation, objectified by skin reflectance, were on the inside of the upper arm treated with a total of six hexagonal areas by an argon laser (AL, 488 nm) and a copper vapor laser (CVL, 578nm). The lasers were connected to a Hexascan device, and physical parameters were identical for 10 the two laser types, except for the wavelengths. Beam diameter was 1 mm, pulse duration 200 msec, intensities 0.7, 1.0, and 1.3 W/spot, resulting in the following spot doses 17.8, 25.5, and 33.1  $J/cm^2$ .

A correlation was demonstrated between pre-treatment skin pigmentation and the clinical effects obtained immediately after and 6 months 15 after the laser treatment. Assessment of the chronic response was based on distinction between pigmentary changes and scarring.

The CVL induced a significantly higher degree of acute results at the 0.7 and 1.0 W/spot treatment level as compared with the AL. For the clinical response 6 months after the laser treatment it turned out that 20 the AL at the 1.0 and 1.3 W/spot induced a significantly higher degree of hyperpigmentation and scarring as compared with the CVL.

An inverse relation was found between the degree of pre-treatment pigmentation and the threshold intensities required to induce wound formation, scar formation and postinflammatory hyperpigmentation, respec-25 tively.

Detailed measuring results obtained by the above test are illustrated in the diagrams 15A-15L.

In Fig. 16, a diagram is shown, illustrating the relation of using the degree of skin pigmentation as a predictor of minimal phototoxic 30 dose to be given to the same individual. The diagram represents the result of the following test or experiment.

Fourteen individuals with skin type (II) (11) and skin type III (3) participated in the test. The sensitivity to irradiation with Philips TL12 tubes was determined without medication on previous unexposed but-35 tocks (MED). The sensitivity to irradiation with Philips TL09 tubes was determined 1 h after oral administration of (0.44-0.63 mg/kg) 8-MOP in a similar way (MPD). The pigmentation of the test areas before irradiation was quantitated with an apparatus according to the present invention,

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the erythema reaction was assessed clinically using a (+)-+++ scale 24 h after TL12, and 72h after TL09 exposure.

The pigmentation % of the unexposed test areas vs. the energy needed to elicit MED or MPD was plotted in scattergrams. There was a positive relation between pigmentation and the dose of TL12 needed to elicit a (+) or + erythemal reaction. The lines of the (+) and + reaction had identical slopes. Similar results were observed with TLO9 exposure after ingestiona of 8-MOP. Spearmanns test for correlation between pigmentation and dose to erythemal reaction was significant for the + reac-10 tion after TL12 exposure, p<0.05. The correlation coefficient for the other parameters was non-significant (0.4>p>0.05).

A further experiment was made:

Seventeen volunteers were tested with Philips TL12 and TL01 tubes on previous unexposed buttocks. Biological doses ranging from 0.25 to 15 3.00 B-MEDs were used.

B-MED derived from the erythema action spectrum of McKinlay and Diffey and 1 MED = 312  $J/m^2$  at 296 nm (Parrish). The physical doses corresponding to 1 B-MED are 0.62  $J/m^2$  for the TLO1 tube and 0.082  $J/m^2$  for the TL12 tube (TL12:TL01 - 1:7.5).

The redness % and pigment protection factor (PPF) were measured be-20 fore and 24 h after exposure with an apparatus according to the present invention. Also the test sites were evaluated clinically after 24 h. Test sites with redness %>30 measured by the apparatus or clinical redness ((+)-+++) were included in the study. The results were given as 25 redness % as a function of dose. Since a linear reciprocity between PPF before exposure and dose to give a specific effect is assumed to exist, the results were also given as redness % as a function of dose/PPF. As the intercept of the four lines did not differ significantly, a common intercept of 22.5 was used.

Since identical biological doses were given of the TL12 and TL01, an identical redness was expected. However, it was found that the dose ratio between TL12 and TL01 to obtain the same redness values was 1:0.55, the TL01 being 1.85 times stronger than TL12. The results are in accordance with the assumption that a linear reciprocity between PPF and 35 the dose needed to produce a specific response exists, since it was found that 1 MED/PPF from the TL12 tube resulted in a redness of 37.1%, not significantly different from the expected 36.9%, the value corresponding to the clinical reading +.

In Fig. 17, a diagram is shown illustrating the correspondence or the difference between experimentally found UV doses and doses calculated to reach a certain redness. The diagram is based on measuring results obtained from the same 49 individuals investigated and used for the experiments or tests on basis of which the diagram shown in Fig. 6 is derived.

In Fig. 18, a diagram is shown, which diagram illustrates the adaptation of the present invention as to determining the sensitivity of an individual who has been exposed to UV treatment. The individual has after determination of the individual's ability to stand exposure to UV radiation, by employing the method and the apparatus according to the present invention, been exposed to UV treatment, i.e. been exposed to a specific UV dose. After the UV treatment, the redness of the individual is as discussed above with reference to Fig. 8 determined. The redness % is converted into a B-MED measure or difference at + redness and ++ redness, which B-MED measure represents the difference between the UV dose to which the individual has been exposed, and the UV dose which the individual may stand.

# **DEFINITIONS**

B-MED Basic Minimal Erythema Dose is 312  $J/m^2$  at 296 nm.

((24 h erythema) Parrish).

5

MED Minimal Erythema Dose for an individual 24 h

after exposure.

dass

PPF

 $PPF \times B-MED = MED$ 

10

The Pigment Protection Factor is the number of B-MEDs

which elicit + redness in an individual 24 h after

exposure.

Erythema Action Spectrum: CIE (McKinlay & Diffey).

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**CLAIMS** 

1. A method of determining an individual's ability to become tanned or to stand exposure to ultraviolet radiation without causing a skin reaction, such as skin cancer or erythema, comprising the following steps:

exposing at least part of said individual's skin surface to electromagnetic radiation of a first wavelength and of a predetermined intensity, said first wavelength being a wavelength at which erythrodermic skin reflection is high,

measuring the intensity of electromagnetic radiation reflected from said part of said individual's skin surface so as to determine a first coefficient of reflection of said skin surface part to said electromagnetic radiation of said first wavelength,

exposing said skin surface part to electromagnetic radiation of a 15 second wavelength and of a predetermined intensity, said second wavelength being a wavelength at which erythrodermic skin reflection is low,

measuring the intensity of electromagnetic radiation reflected from said part of said individual's skin surface part so as to determine a second coefficient of reflection of said skin surface part to electromagnetic radiation of said second wavelength,

comparing said first and second coefficients of reflection with sets of coefficients of reflection representing coherent sets of coefficients of reflection of said first and second wavelengths of specific states of redness so as to determine said individual's skin surface part's state of redness, converting said first and second coefficients of reflection into a set of corrected first and second coefficients of reflection of a specific state of redness, so as to determine said individual's skin surface part's coefficients of reflection of said first and second wavelengths at a specific state of redness, and

converting said corrected first coefficient of reflection into a measure representing said individual's ability to become tanned or to stand exposure to ultraviolet radiation without causing said skin reaction.

- 2. A method according to Claim 1, further comprising the step of determining said individual's skin surface part's degree of pigmentation from said corrected first and second coefficients of reflection of said first and second wavelengths at said specific state of redness.
  - 3. A method according to Claims 1 and 2, said specific state of

redness corresponding to an average zero blood flow state.

4. A method according to any of the Claims 1-3, further comprising the steps of:

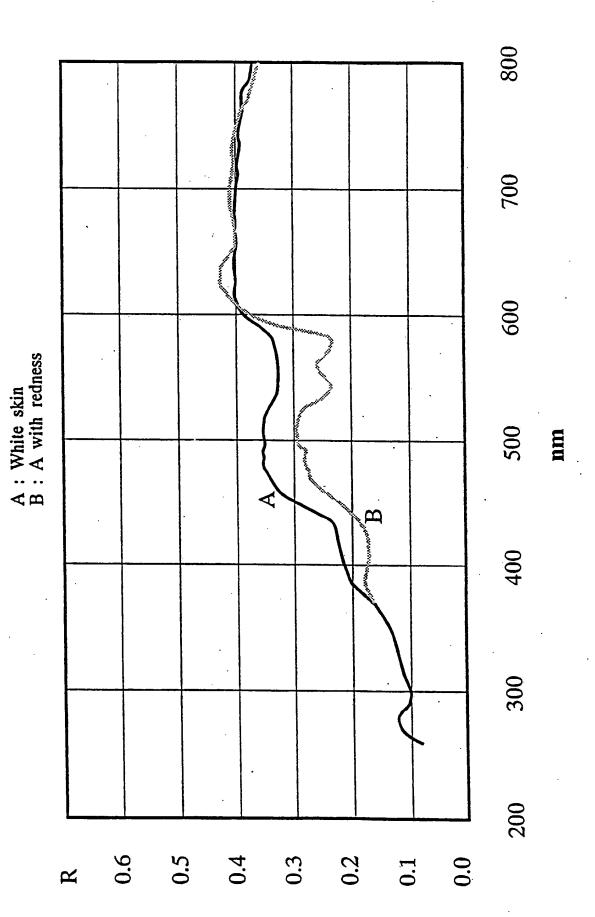
converting said second coefficient of reflection into logarithmic representation, and said sets of coefficients of reflection representing coherent sets of coefficients of reflections of said first and second wavelengths comprising coefficients of reflection of said second wavelengths presented in logarithmic representation.

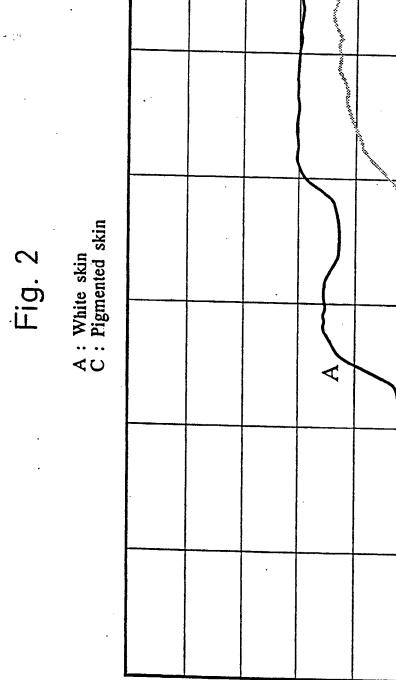
- An apparatus for determining an individual's ability to become tanned or to stand exposure to ultraviolet radiation without causing a skin reaction, such as skin cancer or erythema, comprising:
- a first electromagnetic source for generating electromagnetic radiation of a first wavelength and of a predetermined intensity and for directing said electromagnetic radiation of said first wavelength to a part of said individual's skin surface so as to expose said part of said individual's skin surface to said electromagnetic radiation of said first wavelength,
- a second electromagnetic source for generating electromagnetic radiation of a second wavelength and of a predetermined intensity and for directing said electromagnetic radiation of said second wavelength to said part of said individual's skin surface so as to expose said part of said individual's skin surface to said electromagnetic radiation of said second wavelength,
- a light-detecting means for measuring the intensity of electromag-25 netic radiation reflected from said part of said individual's skin surface,
- a measuring means connected to said light-detecting means for measuring the intensity of electromagnetic radiation reflected from said part of said individual's skin surface so as to determine a first and a second coefficient of reflection of said skin surface part to said electromagnetic radiation of said first and second wavelength, respectively,
- a comparison and converting means connected to said measuring means for comparing said first and second coefficients of reflection with sets of coefficients of reflection representing coherent sets of coefficients of reflection of said first and second wavelengths of specific states of redness so as to determine said individual's skin surface part's state of redness, for converting said first and second coefficients of reflec-

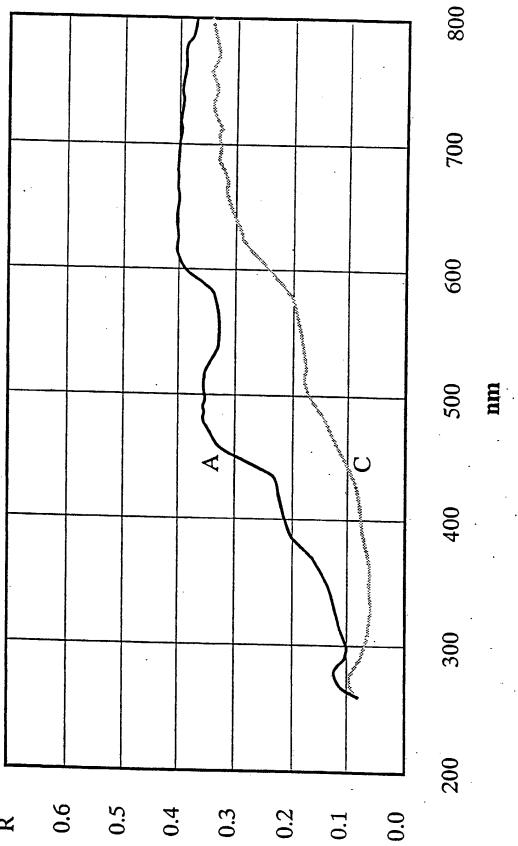
tion into a set of corrected first and second coefficients of reflection of a specific state of redness, so as to determine said individual's skin surface part's coefficients of reflection of said first and second wavelengths at a specific state of redness, and for converting said corrected first coefficient of reflection into a measure representing said individual's ability to become tanned or to stand exposure to ultraviolet radiation without causing said skin reaction.

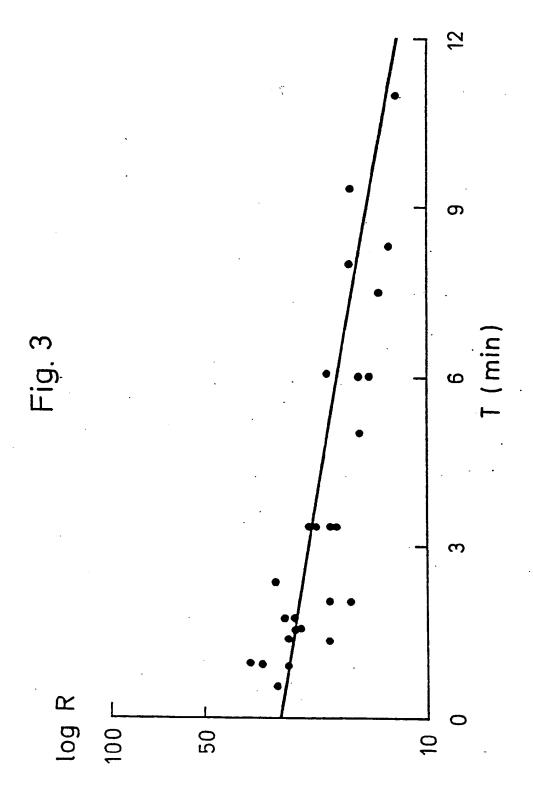
- 6. An apparatus according to Claim 5, said light-detecting means comprising separate first and second light detector means for detecting
   10 electromagnetic radiation of said first and second wavelengths, respectively, reflected from said part of said individual's skin surface part.
- 7. An apparatus according to any of the Claims 5-6, said comparison and converting means further determining said individual's skin surface part's degree of pigmentation from said corrected first and second coefficients of reflection of said first and second wavelengths at said specific state of redness.
  - 8. An apparatus according to any of the Claims 5-7, said specific state of redness being an average Zero blood flow state.
- 9. An apparatus according to any of the Claims 5-8, said comparison and converting means further converting said second coefficient of reflection into logarithmic representation, and said sets of coefficients of reflection representing coherent sets of coefficients of reflection of said first and second wavelengths comprising coefficients of reflection of said second wavelengths represented in logarithmic representation.
  - 10. An apparatus according to any of the Claims 5-9, said first wavelength being of the order of 660 nm, and said second wavelength being of the order of 550 nm.

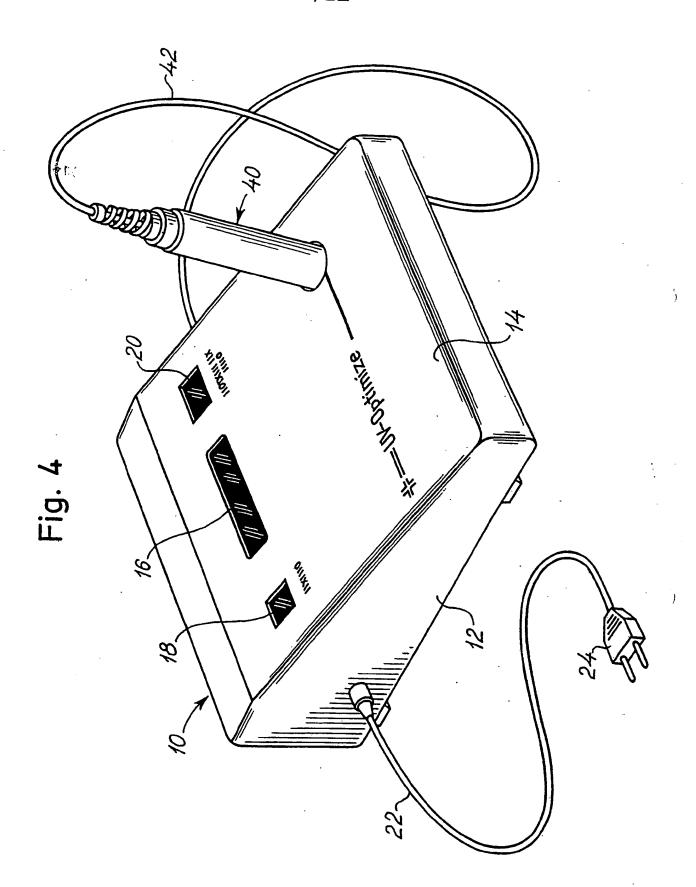
Fig. 1

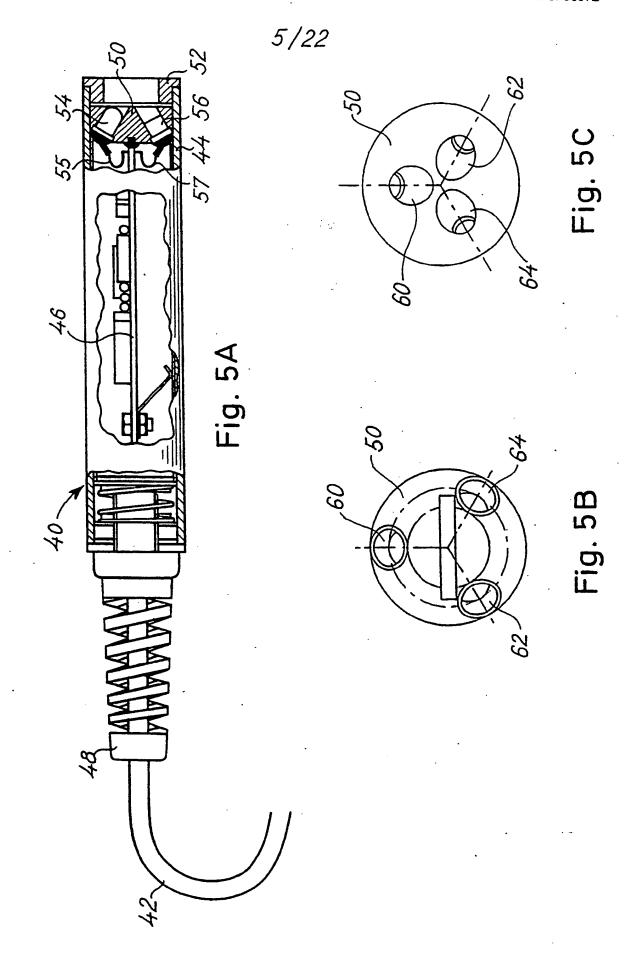




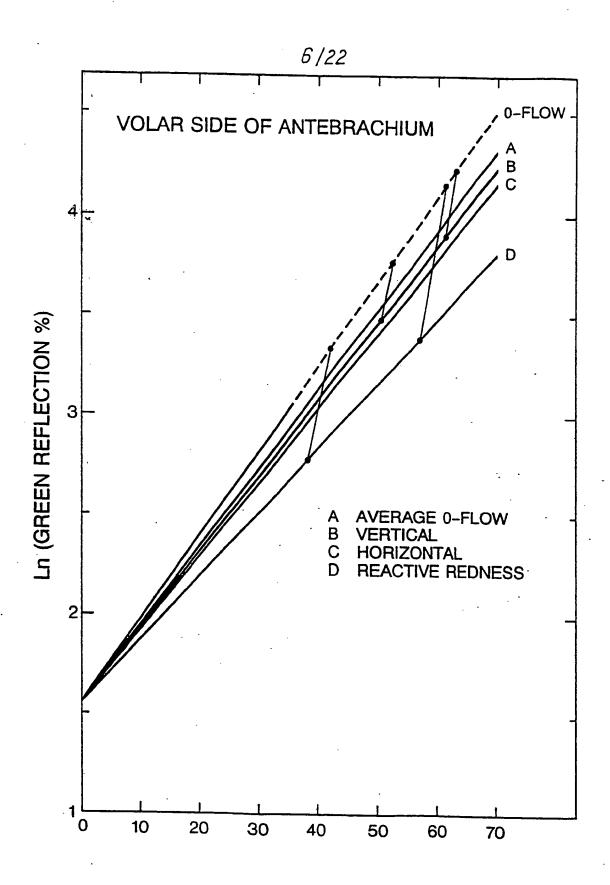


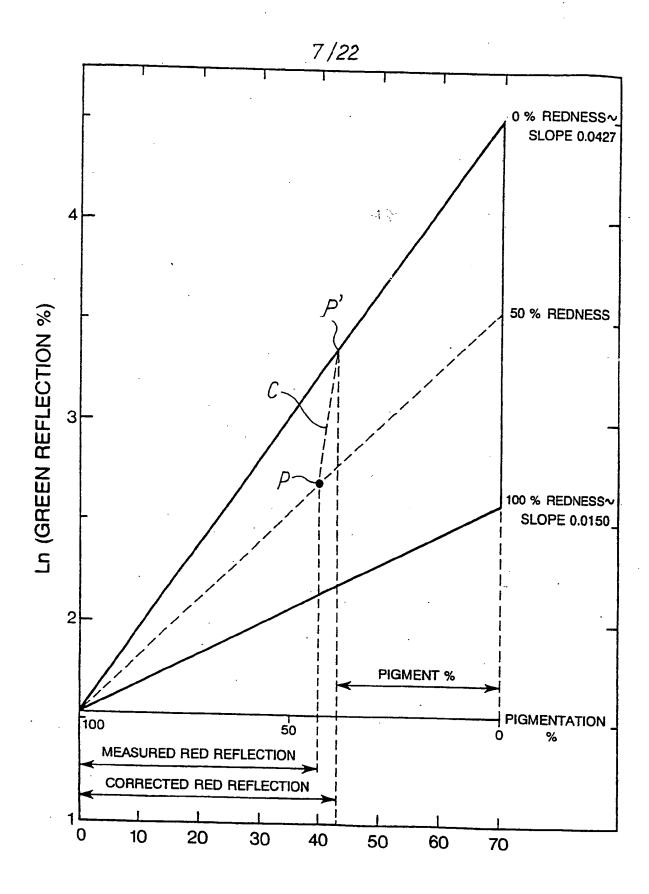


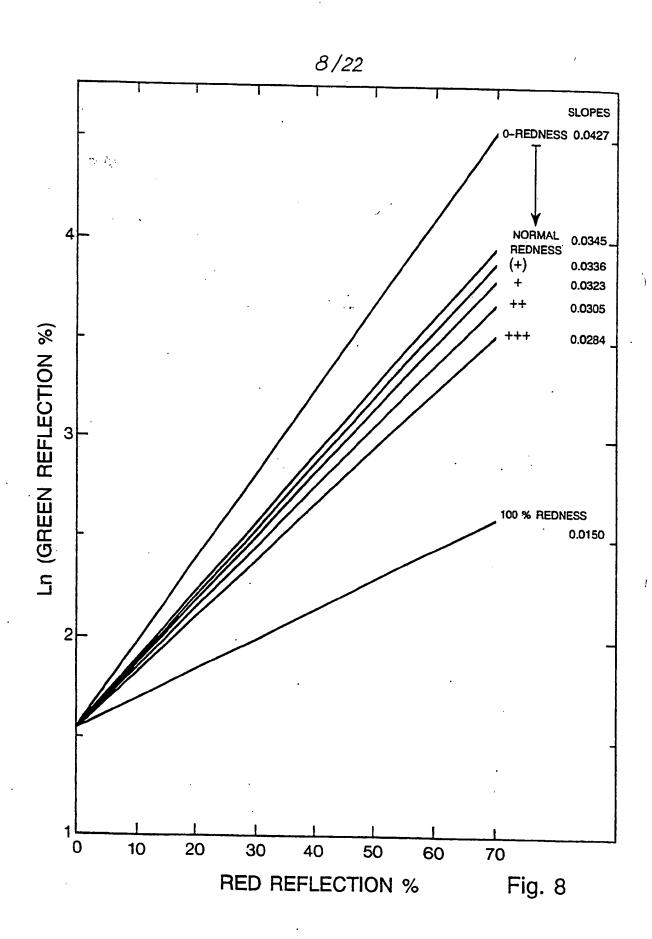


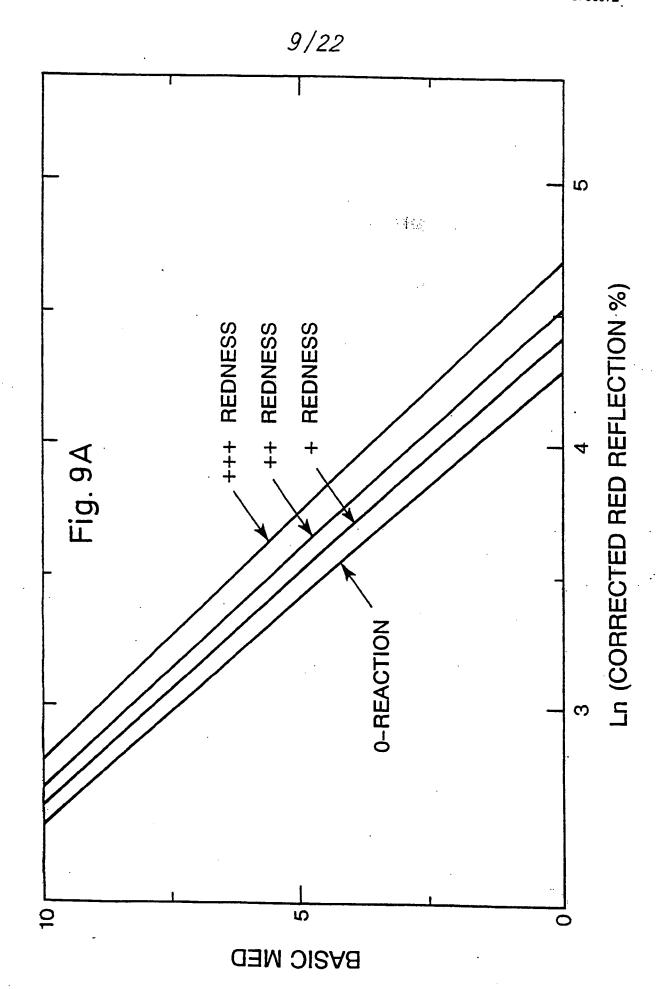


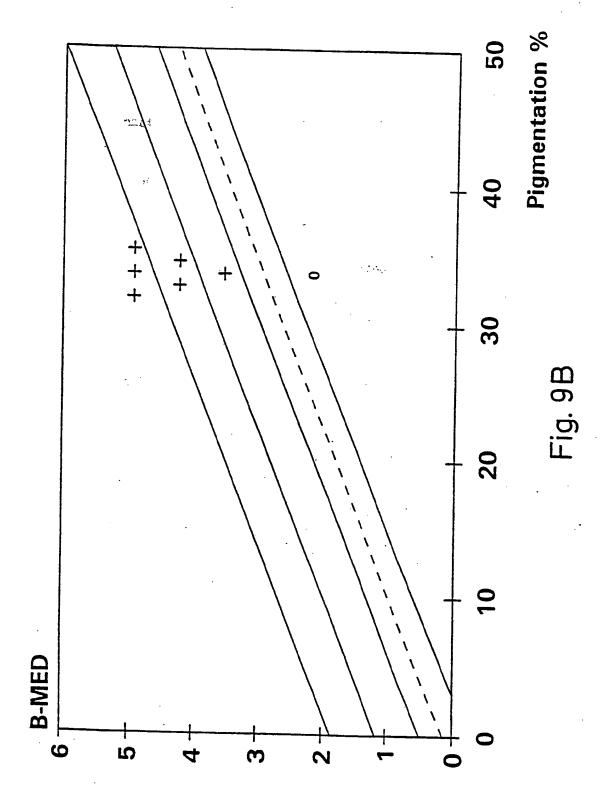
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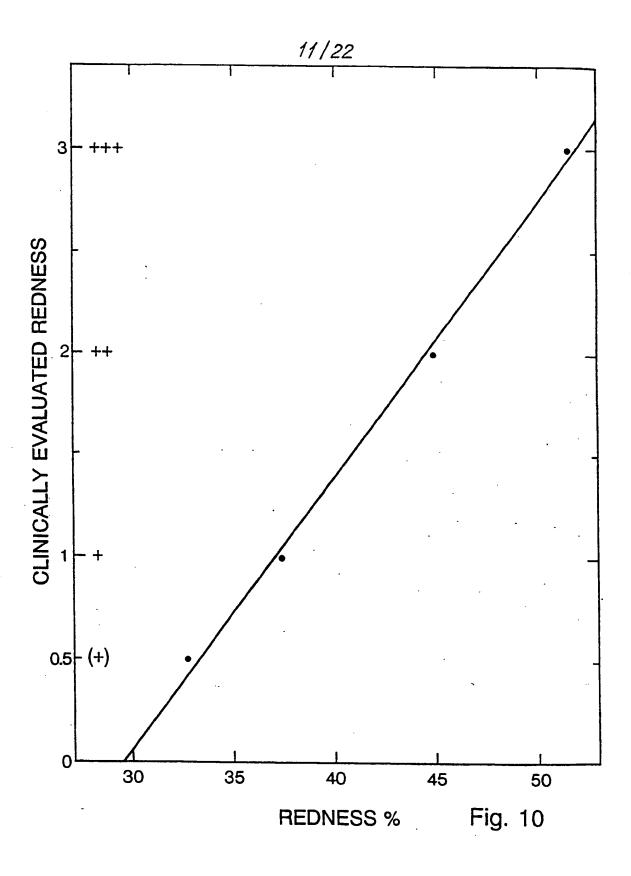




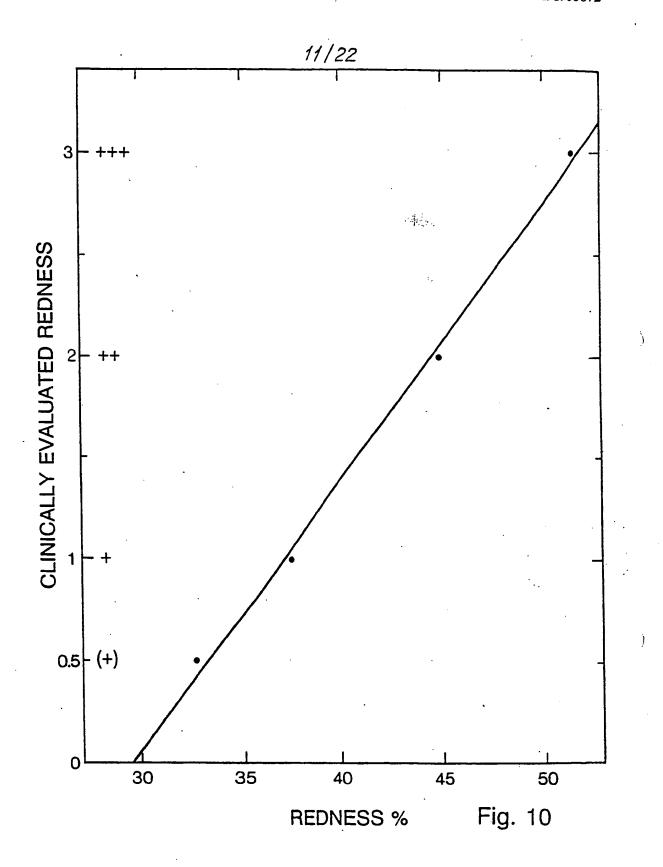


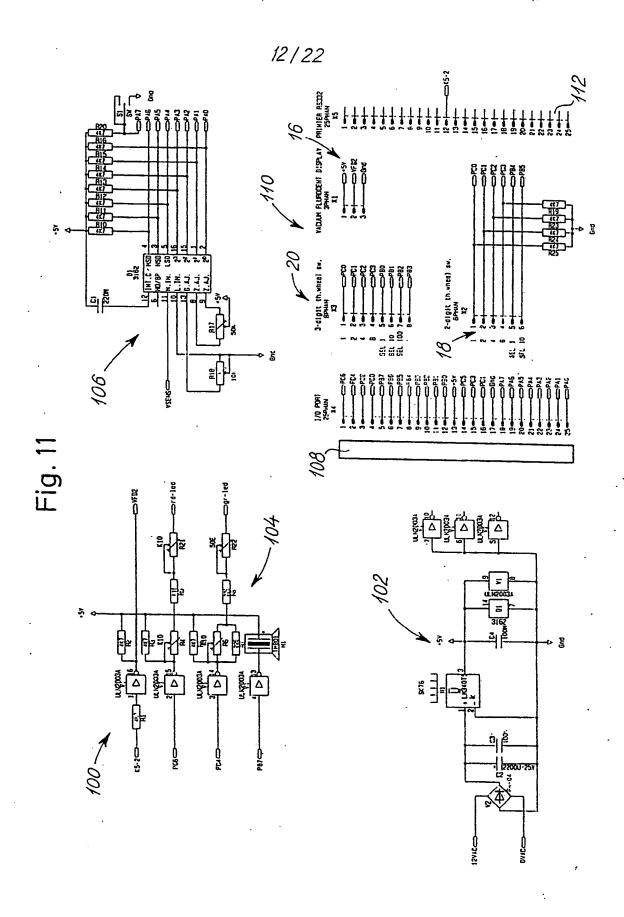




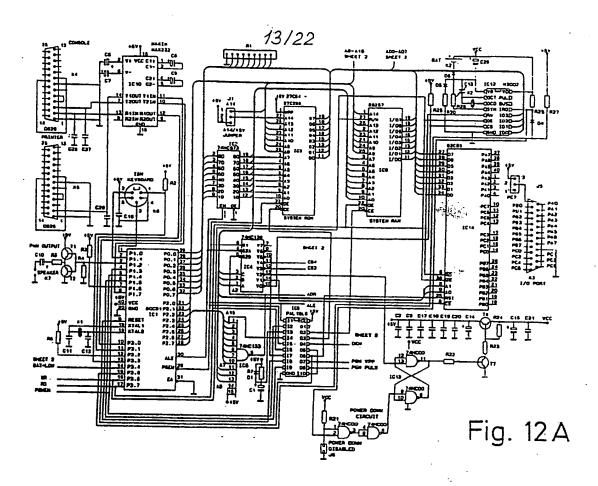


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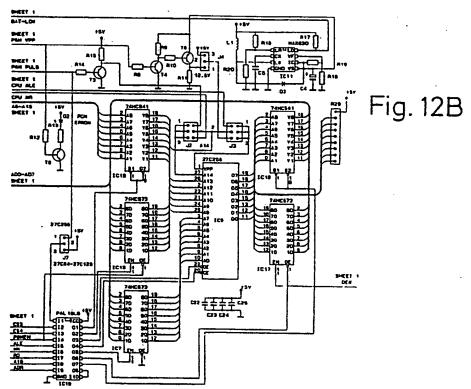
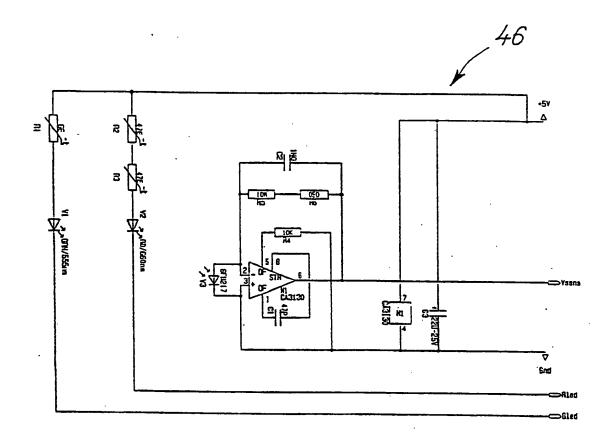
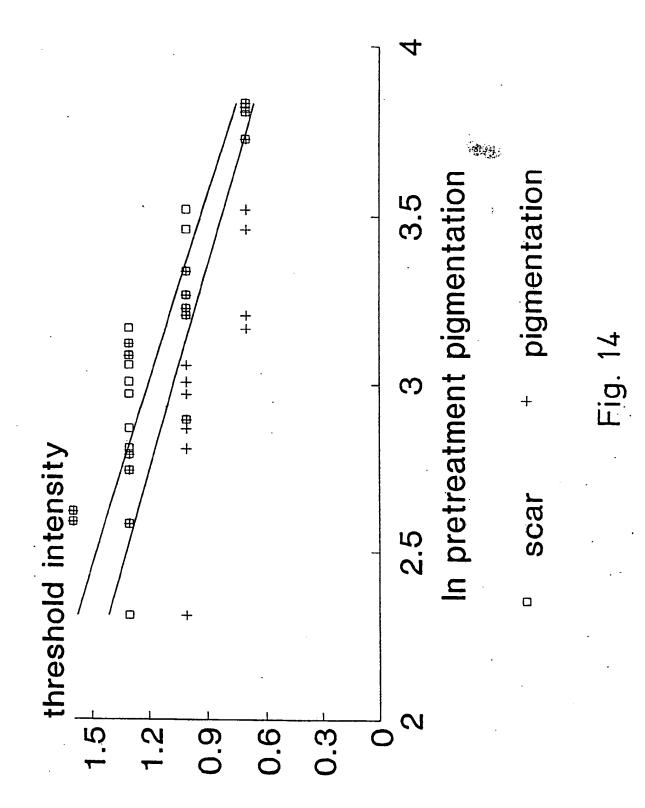


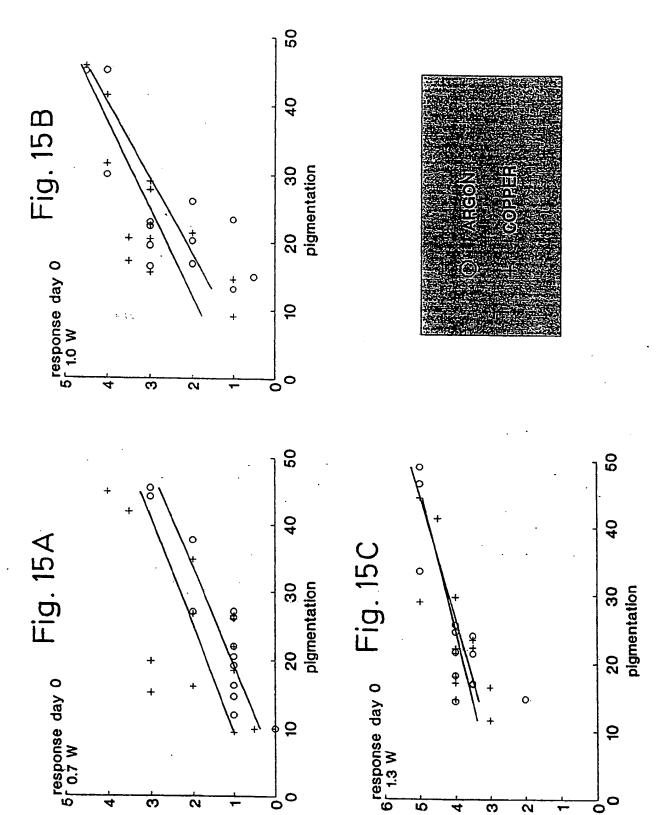
Fig. 13





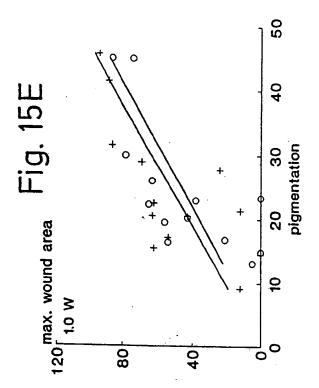
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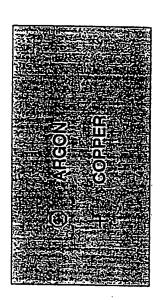
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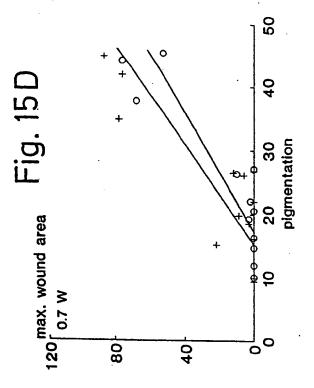


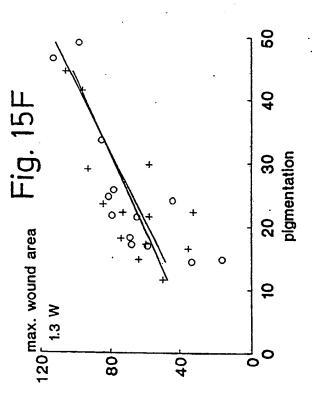
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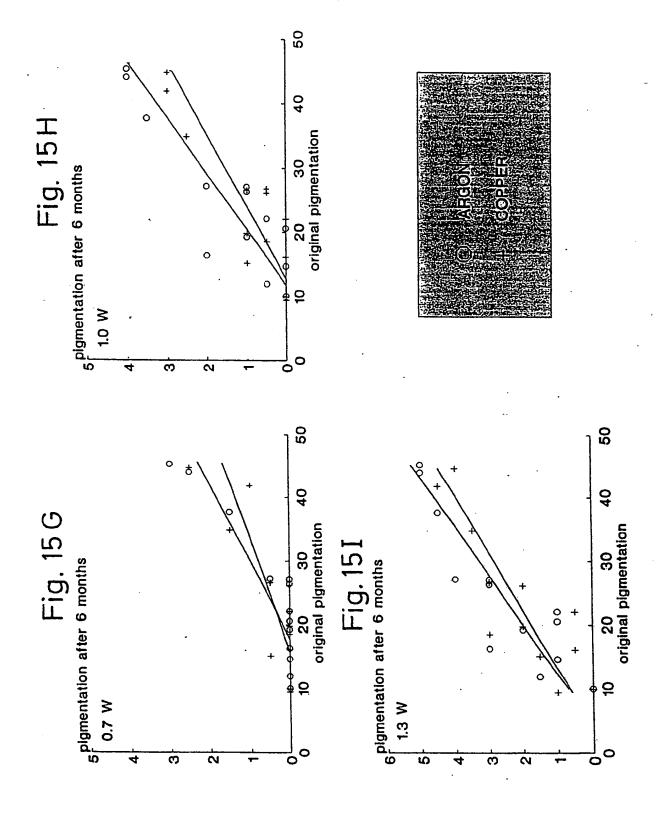
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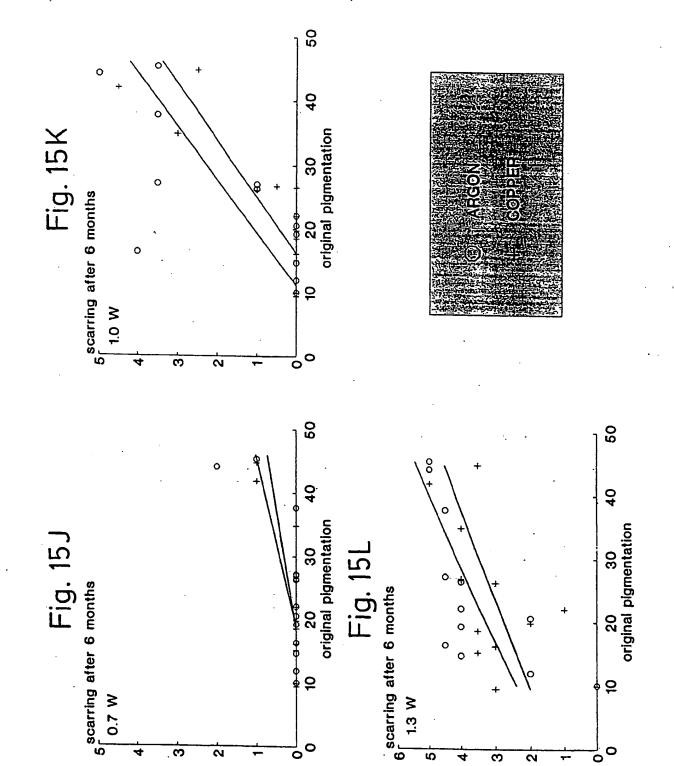












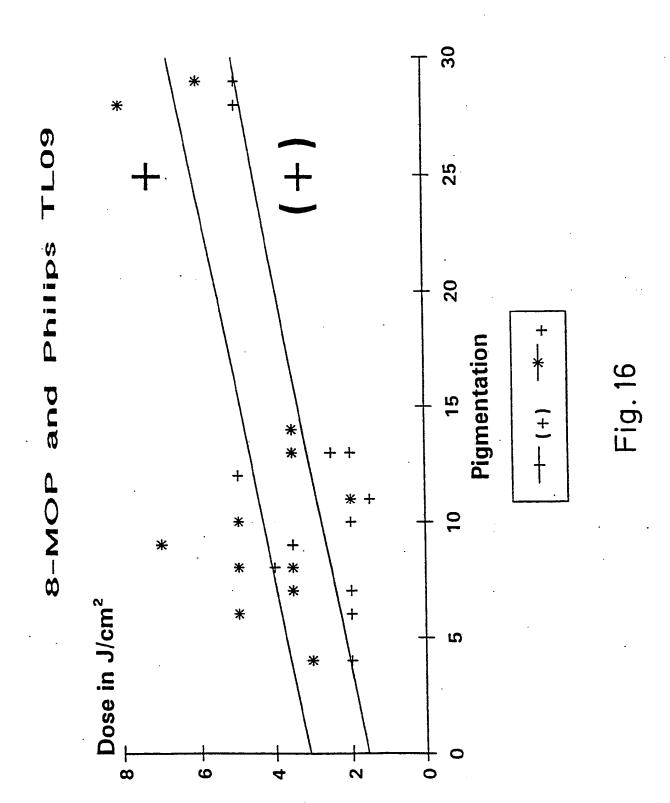
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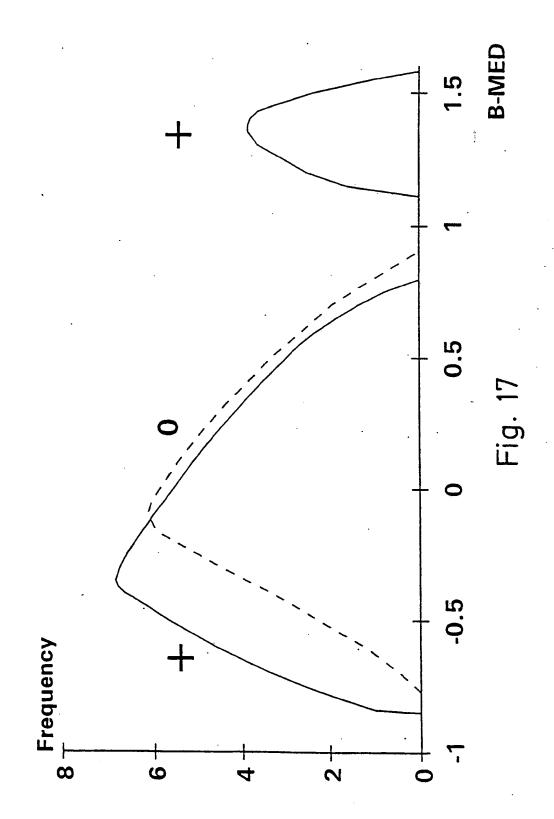
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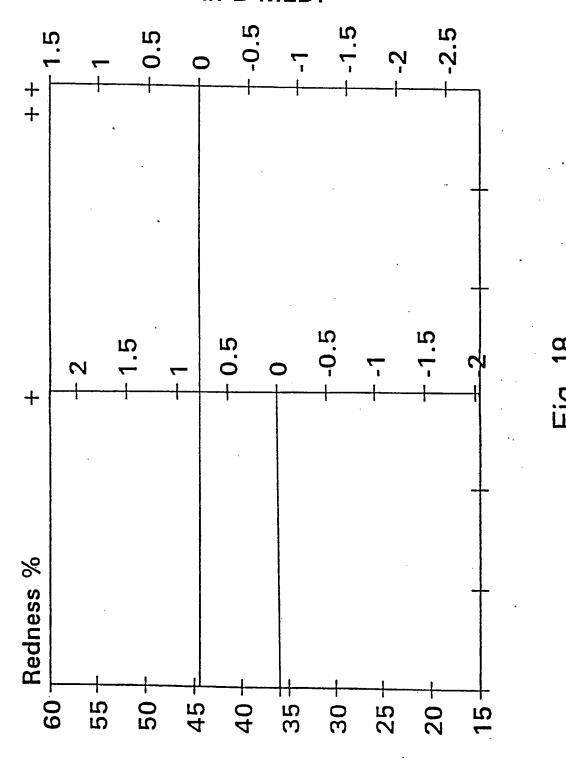
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Difference between experimentally found dose and calculated dose to reach a certain redness.



Sensitivity compared to normal in B-MED.



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#### INTERNATIONAL SEARCH REPORT

International application No.

PCT/DK 93/00072

See patent family annex.

## A. CLASSIFICATION OF SUBJECT MATTER

IPC5: A61B 5/103, G01J 3/50
According to International Patent Classification (IPC) or to both national classification and IPC

#### B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Further documents are listed in the continuation of Box C.

#### IPC5: A61B, G01J

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

# SE,DK,FI,NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

	JMENTS CONSIDERED TO BE RELEVANT	
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US, A, 4882598 (HANS C. WULF), 21 November 1989 (21.11.89), claim 6	1-10
	<b></b>	
A	US, A, 4423736 (DAVID P. DEWITT ET AL), 3 January 1984 (03.01.84), abstract	1-10
	<b></b>	
<b>A</b> .	US, A, 4749865 (KLAUS SCHELLER), 7 June 1988 (07.06.88), see the whole cocument	1-10
A	US, A, 4846184 (ALAIN COMMENT ET AL), 11 July 1989 (11.07.89), see the whole document	1-10
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the priority date claimed	"&" document member of the same patent family			
Date of the actual completion of the international search	Date of mailing of the international search report			
17 May 1993	· <b>0 1</b> -06- 1993			
Name and mailing address of the ISA/	Authorized officer			
Swedish Patent Office	Addionized officer			
Box 5055, S-102 42 STOCKHOLM	Amdana II. 7			
Facsimile No. +46 8 666 02 86	Anders Holmberg			
	Telephone No. +46 8 782 25 00			
form PCT/ISA/210 (second sheet) (July 1992)				

# INTERNATIONAL SEARCH REPORT

International application No.
PCT/DK 93/00072

·	PO	CT/DK 93/00072
	nation). DOCUMENTS CONSIDERED TO BE RELEVANT	
Category*	Citation of document, with indication, where appropriate, of the relevan	nt passages Relevant to claim No
	WO, A1, 8805284 (NEWER S.A.), 28 July 1988 (28.07.88), see the whole document	1-10
\	WO, A1, 9114159 (HENRIK LEMMING), 19 Sept 1991 (19.09.91), see the whole document	1-10
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# INTERNATIONAL SEARCH REPORT Information on patent family members

31/03/93

International application No. PCT/DK 93/00072

Patent document cited in search report		Publication Patent family date member(s)			Publication date
IS-A- 4	882598	21/11/89	EP-A- WO-A-	0238574 8701948	30/09/87 09/04/87
JS-A- 4	423736	03/01/84	NONE		;
JS-A- 4	749865	07/06/88	DE-A,C- EP-A-	3506690 0193163	04/09/86 03/09/86
JS-A 4	846184	11/07/89	EP-A,B-	0198759	22/10/86
/O-A1- 8	8805284	28/07/88	AU-A- CH-A,B- EP-A-	1104588 669325 0301042	10/08/88 15/03/89 01/02/89
/O-A1- 9	114159	19/09/91	AU-A-	7468391	10/10/91

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